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(54) Title: NEW PRODUCTS SPECIFIC TO PATHOGENIC STRAINS AND THEIR USE AS VACCINES AND IN IMMUNOTHERAPY

(57) Abstract: The invention relates to isolated antigenic polypeptides obtainable by a process comprising the steps of: 1- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria, 2- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates, 3- purifying the polypeptides identified in step 1, which are found in step 2 to be conserved in B2/D isolates, 4- testing the polypeptides for immunogenicity using animals models. Application for making vaccines compositions and immunotherapies

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New products specific to pathogenic strains and their use as vaccines and in immunotherapy

The invention relates to new products specific to pathogenic strains, particularly to extra-intestinal *E. coli* strains.

It more particularly relates as products to antigenic polypeptides and antibodies directed against said polypeptides and to their use as vaccines and in immunotherapy, respectively.

Although *Escherichia coli* is probably the best known bacterial species and is one of the most common isolated in clinical microbiology laboratories, misconceptions abound regarding the various types of *E. coli* and the infections they cause.

- E. coli strains of biological significance to humans can be broadly classified in 3 major groups:
 - 1. Commensal strains, which are part of the normal flora.
- 2. Intestinal pathogenic strains, which are not part of the normal flora. This group contains various pathotypes (EPEC, EHEC, ETEC, EIEC) not including Shigella.
 - 3. Extra-intestinal strains (ExPEC) which are responsible for infections outside the gastro-intestinal (GI) tract, but can also be part of the normal flora. All hosts, either immunocompromised or not are susceptible to these infections.

EXPEC strains are responsible for the majority of the urinary tract infections (UTI) particularly cystitis, pyelonephritis, and cathether associated infections.

They are also responsible for abdominal infections, nosocomial pneumoniae, neonatal meningitidis, soft tissue infections, and bone infections. Each one of these localizations can lead to

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bacteremia with a risk of sepsis in case of organ failure. EXPEC strains are indeed the most common Gram negative bacilliisolated from blood cultures.

5 750 000 cases of bacterial sepsis occur each year in the US, and are responsible for 225 000 deaths. In a recent study on 1690 cases of sepsis, it was shown that the main bacteria species identified is ExPEC (16% of the cases) and then S.aureus (14% of the cases).

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These numbers demonstrate the importance of ExPEC strains in both hospital and community acquired infections.

EXPEC strains correspond to a homogenous subset of *E. coli* strains. Analysis of phylogenetic relationships among *E. coli* strains by MLEE has revealed that *E. coli* belong to 4 main phylogenetic groups designated A, B1, B2 and D.

The pathogenesis of ExPEC strains is that of extra-cellular 20 microorganisms, i.e., they are well adapted to growth in the extra-cellular fluids and efficiently resist phagocytosis by polymorphonuclear. Initial studies have shown that virulence factors known to be important for the extra-cellular growth are mainly found in B2/D E. coli., thus suggesting that B2/D25 subgroups contain most of the ExPEC strains. reinforced by experiments' performed on animals showing that B2/D strains are more virulent than A and B1 Subsequent epidemiological studies have indeed confirmed these hypotheses. B2/D isolates are those predominantly responsible for neonatal meningitidis (87%) and community or nosocomial 30 acquired urosepsis, (93 % and 85%, respectively).

Similar results have been reported for cystitis (70% are due to the sole B2 E. coli), thus demonstrating that the importance of ExPEC strains.

5 These recent findings demonstrate that the B2/D subgroup of strains is the *E. coli* core genome the best adapted to growth in extra-cellular fluids.

In addition to this core genome, ExPEC strains have various pathogenicity islands which encode virulence factors associated with the different pathogenesis of extra-intestinal E. coli infections (UTI, urosepsis, neonatal meningitidis...). Among the main virulence factors are the capsule, which is well-known to be important for extra-cellular growth, and the iron chelation systems (aerobactin and enterochelin, for example). In addition, depending on the pathogenesis, these strains can produce toxins (CNF, hemolysin...), adhesins (pap, sfa...) and other iron chelation systems.

The notion that B2/D E. coli correspond to a distinct subset of pathogenic E. coli strains is reinforced by the fact that B2/D E. coli are not broadly isolated from the stools of humans. They were recovered from only 11% of individuals, whereas A and B1 subgroups are present in the stools of 74% of the individuals of a human population.

As mentioned above the pathogenesis of ExPEC strains relies on their ability to multiply in the extra-cellular fluids and to resist bactericidal activity of the complement and phagocytosis by polymorphonuclear. Therefore, as for other extra-cellular pathogens (Haemophilus influenzae, Streptococcus pneumonieae and Neisseria meningitidis) a protective antigen against ExPEC has to induce antibodies

that promote opsonisation and/or the bactericidal activity of serum.

Considering the above statements, an efficient antigen has to be largely represented among the population of B2/D E. coli. Similarly to other extra-cellular pathogens, the capsular polysaccharide would be an ideal antigen, however most pathogenic B2 strains express the K1 polysaccharide. The latter has a structure identical to that of group B meningococcus, which is non-immunogenic and shares common antigens with the brain. Another possible target may be the lipopolysaccharide (LPS). However there are a large number of different LPS serotypes that are shared by various subgroups.

- The inventors have now found that some specific components coded by the B2/D genome, but absent from A and B1 E. colistrains, are particularly useful as antigens and can specifically prevent the pathologies due to ExPEC strains. Homologs of these antigenic components can be found in other pathogenic bacterial species and therefore are useful to prevent the pathologies caused by these bacteria. Accordingly, any reference to products specific to ExPEC strains and to their uses will encompass components in these species.
- 25. For example homologuous antigens could be present in the following species and be as such used for prevention of disease due to the bacteria:
- Pseudomonas aeruginosa, Escherichia coli 0157:H7, Yersinia pestis, Vibrio cholerae, Legionella pneumophila, Salmonella 30 Salmonella typhimurium, Haemophilus influenzae, Neisseria meningitidis, Neisseria gonorrhoeae, Bacillus anthracis, Burkholderia cepacia, Campylobacter jejuni, Chlamydia pneumoniae, Chlamydia trachomatis,

Clostridium botulinum, Clostridium difficile, Cryptococcus neoformans, Enterobacter cloacae, Enterococcus Helicobacter pylori, Klebsiella pneumoniae, Mycobacterium leprae, Mycobacterium tuberculosis, Pseudomonas aeruginosa, Salmonella paratyphi, Salmonella typhi, Staphylococcus aureus, Klebsiella pneumoniae, Listeria monocytogenes, Moxarella catarrhalis, Shigella dysenteriae, Shigella flexneri, Shigella sonnei, Staphylococcus epidermidis, Streptococcus pneumoniae, and any species falling within the genera of any of the above species.

It is then an object of the invention to provide new isolated antigenic polypeptides, and polynucleotides belonging to the core B2/D genome and not present in commensal *E. coli*.

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Another object of the invention is to provide antibodies raised against such antigenic polypeptides, or peptidic fragments.

20 It is still another object of the invention to provide vectors and host cells containing said polynucleotides.

Another object of the invention is to provide vaccine compositions specific to extra intestinal infections caused by ExPEC and pathologies caused by other pathogenic strains expressing antigenic polypeptides homologous to the ExPEC antigenic polypeptides.

The invention also relates to means for detecting and treating a development of *E. coli* in a human or animal compartment which is extra-intestinal (systemic and non-diarrhoeal infections, such as septicaemia, pyelonephritis, or meningitis in the newborn).

The isolated antigenic polypeptides used according to the invention are selected among polypeptides specific to B2/D E. coli strains and not present in A and B1 isolates of E. coli. They are encoded by genes belonging to the core B2/D genome and are not present in commensal E. coli.

They have a sequence selected in the group comprising the sequences of SEQ ID N°11 to N°66 or 133-145 or homologous sequences with a minimum of 25% of identity with the whole sequences SEQ ID N°11 to N°66, or 133-145, respectively.

The isolated polypeptides having SEQ ID N° 14, 15, 17, 21, 22, 23, 28, 29, 30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52 to 55, 58, 60, 63, 133-138 are new polypeptides and therefore are part of the invention.

The invention also relates to homologous isolated antigenic peptides, comprising polypeptides having at least 25% identity to a polypeptide having a sequence SEQ ID N° as above defined, more particularly having SEQ ID N°14, 15, 17, 21, 22, 23, 28, 29, 30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52 to 55, 58, 60, 63, 133-138, or at least 25% identity to a fragment comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide having a sequence corresponding to said SEQ, ID N°s, as determined using BLASTP or BLASTX with the default parameters.

Said polypeptides are obtainable by a process comprising the $30\,$ steps of :

a- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria,

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b- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates,

- c- purifying the polypeptides identified in step a, which are found in step 2 to be conserved in the B2/D isolates,
- d- testing the polypeptides for immunogenicity using animals models.

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By the term "conserved", it is meant, according to the invention, that the genes coding for the polypeptides are present with a frequency of at least 50% in B2/D isolates, preferably greater than 60%, more preferably greater than 80% and even more preferably greater than 85%, and in less than 40% in A/B isolates, preferably in less than 20%, more preferably in less than 15%.

The animal models used in step c are infected adult animals, eventually immunodepressed.

The adult animals particularly mice, are infected intraperitoneally, the endpoint being the animal death and/or bacteremia measurement.

The animals can be immunodepressed by injection, for example, of cyclophosphamide which induces a neutropenia. Such a model will validate the use of the antigen for prevention of *E. coli* sepsis in immunodepressed patients. Another animal model could be for example 2 to 3 day old infant mice.

The variants or fractionnal sequences conserving the B2/D properties and which are antigenic as defined in step 4 of the above process are also part of the invention. The term "variant" is herein intended to mean any sequence having insertions and/or deletions and/or substitutions with respect

to the parent sequence. The term "fractional" is herein intended to mean any fragment of the parent sequence.

The invention also relates to the use of isolated polynucleotides coding for a polypeptide such as above defined according to the universal genetic code and taking into account the degeneracy of this code. The term "polynucleotide" encompasses any nucleotidic sequence such as DNA, including cDNA, RNA, including mRNA.

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Said polynucleotides have preferably sequences corresponding to SEQ ID N°77 to SEQ ID N°132 or 146 to 158 .

More preferably, said polynucleotides have sequences corresponding to SEQ ID N° 80, 81, 83, 87, 88, 89, 94, 95, 96, 98, 102, 104, 105, 107-110, 112, 115, 116, 118, 119, 126, 127, 130, 132, 135, 146-151.

the homologs to invention also relates to The polynucleotides . Said homologs may have at least 25% identity 20 to a polynucleotide having said sequences, or at least 25% identity to a fragment comprising at least 15, at least 30, at least 60, at least 90, at least 120, at least 150, at least nucleotide 180 more than 180 consecutive polynucleotide having one of said SEQ ID N°s, as determined 25 using BLASTN with the default parameters, and are encompassed by the invention inasmuch as they are capable of coding for a polypeptide having the antigenic properties of those according to the invention.

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The present application is also aimed towards any vector comprising at least one of said polynucleotides and also any cell transformed by genetic engineering, characterized in that it comprises, by transfection, at least one of said

polynucleotides and/or at least one vector according to the invention, and/or in that said transformation induces the production by this cell of at least one polypeptide corresponding to a polynucleotide such as above-defined.

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The invention also relates to a process for isolating and identifying antigenic polypeptides, therefore useful as vaccine for E. coli.

10 Such a process comprises the steps of

- a- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria,
- b- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates,
 - c- purifying the polypeptides identified in step a, which are found in step 2 to be conserved in B2/D isolates,
 - d- testing the polypeptides for immunogenicity using animals models.

The selected antigenic polypeptides, alone or in combination, are capable of inducing an antibody response for prevention of infections due to ExPEC strains regardless of the pathogenesis and of the infection site (UTI, pyelonephritis, sepsis, bacteremia, neonatal meningitis).

Such polypeptides particularly have sequences SEQ ID $N^{\circ}1$ to SEQ ID $N^{\circ}66$, or 133-145 or correspond to homologous sequences.

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The invention thus relates to vaccine compositions specific to E. coli extra-intestinal infections, comprising an effective amount of at least one antigenic polypeptide or fragment thereof as above defined, with a carrier, particularly at

least one polypeptide of SEQ ID N°1 to SEQ ID N°66, except SEQ ID N°8, and 133-145 and the homologous polypeptides.

Such vaccine compositions are particularly useful for preventing urinary system infections, pyelonephritis, sepsis, bacteremia, neonatal meningitis.

The vaccine compositions of the invention are indicated for :

- immunodepressed patients, ideally before the start of the immunosuppressive therapy: patients suffering from cancer, diabetes, leukaemia, transplant patients, patients receiving long-term steroids therapy.
 - Patients before surgery where there is a high risk of E. coli infections (abdominal surgery).
 - In all these cases, the *E. coli* vaccine of the invention could be administered in association with a Staphylococcus aureus vaccine,
 - Patients with recurrent UTI, especially after one episode of pyelonephritis.
 - The prevention of neonatal infections will require vaccination of the mother, implying vaccination long before pregnancy to avoid potential problem. Ideally such a vaccine should be associated with a Group B Streptococcus polysaccharide vaccine in order to also prevent late onset neonatal infections. It should be pointed out that the induction of a level of antibodies against B2/D E. coli in pregnant women would also prevent UTI, which are always a risk in the context of a pregnancy.

The formulation and the dose of said vaccine compositions can be developed and adjusted by those skilled in the art as a function of the indication targeted, of the method of

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administration desired, and of the patient under consideration (age, weight).

These compositions comprise one or more physiologically inert vehicles, and in particular any excipient suitable for the formulation and/or for the method of administration desired.

For example the vaccine could be a suspension of the purified polypeptide in sterile water with aluminium based miniral salt as adjuvant and be administred subcutanously with a first and boosting injection.

The antibodies raised against the above-identified polypeptides are also part of the invention.

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They are capable of binding to said polypeptides physiological-type conditions (in vivo or mimicking in vivo) when administered to a human or animal organism, and ELISAtype conditions when said binding product is intended to be assays and methods in vitro. Such advantageously inhibit the extra-intestinal growth of ExPEX strains in human or animal.

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They are particularly useful for immunotherapy applications with antibodies specific to polypeptidic antigens, for treatment and prevention, of severe infections in at risk populations such as neonates or patients undergoing surgical procedures. For these applications specific human monoclonal antibody (Mab) will be derived from the peptides or polypeptides.

The methods for manufacturing such antibodies using the polypeptides according to the invention are available to those skilled in the art. They are conventional methods which

comprise, in particular, the immunization of animals such as rabbits and the harvesting of the serum produced, followed optionally by the purification of the serum obtained. A technique suitable for the production of monoclonal antibodies is that of Köhler and Milstein (Nature 1975, 256:495-497).

Said antibodies do not recognize the cells of the human or animal to which it is intended.

In particular for immunotherapy applications with monoclonal antibodies specific to polypeptidic antigens, for treatment and prevention of severe infections in at risk populations such as neonates or patients undergoing surgical procedures. For these applications specific human monoclonal antibody will be derived from the peptides or polypeptides.

The antibodies or fragments thereof are advantageoulsy humanized when intended for a human administration.

Alternatively, humanized Mab could be derived from murine or rat Mab specific of the antigen. These fully humanized Mab are constructed using conventional molecular techniques to graft complementarity-determining regions from the parent murine or rat antibacterial antibody into human IgG1 kappa heavy and light-chain frameworks.

The present invention is also aimed towards the use, in an effective amount, of at least one of polypeptides having SEQ ID N°14, 15, 17, 21, 22, 23, 28, 29, 30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52 to 55, 58, 60, 63, 133-138, antibodies or polynucleotides for the diagnosis of the presence or absence of undesirable extra-intestinal *E. coli*, and/or for the diagnosis of an extra-intestinal *E. coli* infection.

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The detection of the presence or absence of such compounds can in particular be carried out by nucleotide hybridization, by PCR amplification or by detection of their polypeptide products. Detection of the presence of such compounds makes it possible to conclude that a B2/D E. coli strain is present.

The invention also relates to pharmaceutical compositions for alleviating and/or preventing and/or treating an undesirable growth of $E.\ coli$ comprising an effective amount of at least one polypeptide as above defined, particularly having SEQ ID N°1-66 to 133-145, in combination with a pharmaceutically acceptable carrier.

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Preferred pharmaceutical compositions comprise at least one polypeptide having SEQ ID N°14, 15, 17, 21, 22, 23, 28, 29, 30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52 to 55, 58, 60, 63, 133-138,

The present application is also aimed towards any use of a polypeptide such as above defined for the manufacture of a composition, in particular of a pharmaceutical composition, intended to alleviate and/or to prevent and/or to treat an undesirable growth of E. coli, such as an E. coli infection, (for example systemic and non-diarrhoeal infections), the presence of extra-intestinal E. coli or a sanitary contamination.

The present invention is illustrated by the examples which follow and which are given in a non limiting capacity and with reference to figures 1 and 2, wherein

- Figure 1 represents a protein purification result after cloning and expression, and

- Figure 2 is a picture of the DNA array after hybridization with the genomic DNA from a B2/D reference strain.

- 5 Example 1: Assay for the immunogenicity of a selected polypeptide from sequences 1-66 and 133-145 (except SEQ ID N°8)
- . Cloning expression and purification of the selected 10 polypeptide.

The nucleic acid having SEQ ID N°95 encoding the polypeptide corresponding to SEQ ID N°28 was cloned without the signal sequence (coding the 16 first amino acids) in a prokaryotic expression vector according to classical methods for cloning. The recombinant plasmid was used to transform the $E.\ coli$ strain BL21. Transformed cells containing the recombinant plasmid were selected in LB medium with $100\mu g/ml$ ampicillin. Individual clones are picked and grown in presence of IPTG 1mM to induce recombinant protein expression. Total protein content of the culture cells was extracted by cell lysis. Recombinant protein was purified by affinity columns.

Protein purification after cloning and expression

Total cell lysat of IPTG-induced bacteria were mixed with Ni-NTA matrix (Qiagen®) for 60 min et 4°C and loaded into a column. After washing the column to remove non specific binding, the recombinant protein was eluate 3 times with 1 ml elution buffer pH 5.9. The protein was then eluate 4 times with 1 ml elution buffer pH 4.5.

Figure 1 represents a Coomassie blue stained SDS gel of recombinant protein after affinity column purification: PM:

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markers E1-4: sample collected from each purification fraction. Arrow indicate the band corresponding to the recombinant protein.

5 . Test for immunogenicity in an animal model

Polypeptide preparation from SEQ ID N°28 was injected to Swiss mice to induce an antibody response as follows:

- 10 At d0 a first immunisation was done by injecting $20\mu g$ of the protein at in $100\mu g$ solution of PBS and complet Freund adjuvant (1:1). Control animals were injected with $100\mu l$ solution of PBS and complet Freund adjuvant (1:1).
- 15 Boosting injection at d21 with $10\mu g$ of protein in $100\mu l$ PBS and complet Freund adjuvant (1:1).

Sera from vaccinated animals was prepared from blood drawn by puncture in the tail of the mice.

Detection of specific antibodies in animal sera, at d20 before the boosting injection, was performed by western blot according to standart protocol. Purified polypeptide was subjected to electrophoresis (10 μ g per lane) and transfert to

25 nitrocellulose membrane.

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The membranes were then saturated by incubation 35 min with PBS/Tween20 0.1%/powder milk 5%.

Diluted sera was incubated with the membrane for 45 min. Membranes were washed three time 5 min with PBS/tween. Bound antibodies were then recognized by an anti-mouse IgG coupled to horseradish peroxidase enzyme. After washing 3 times with PBS/Tween and 3 time with PBS, enzymatic activity was revealed

by addition of chromogenic substrate DAB and hydrogen peroxyde.

Results: Sera from vaccinated animal, diluted at 1/100 revealed a unique band corresponding to the injected polypeptide. No antibody to the polypeptide could be detected in sera from control animals.

At d42, 300 μ l of cyclophosphamide and 200 μ l at d45 were injected IP in the mice to induce neutropenia in order to increase the susceptibility to the challenge infection.

At d46 vaccinated and control mice were challenged by intraperitoneal injection of the wt B2/D strain C5 of $E.\ coli$ at a dose equal to 10 time the LD50 (letal dose).

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Immunogenicity of the selected polypeptide and protection conferred by vaccination with the seleted polypeptide was assessed by the survival of vaccinated animals three days post challenge.

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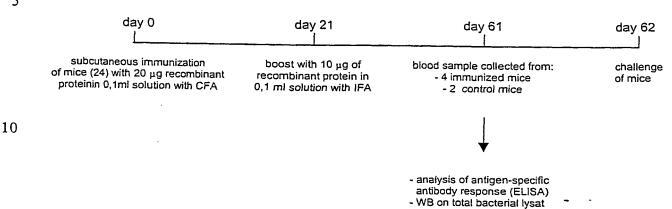
Another example of vaccination to demonstrate immunogenicity of polypeptides:

- 24 Balb/c mice, female, 6 weeks old were immunized by subcutaneous Injection of the protein in Complete Freund's adjuvant, and 14 control mice were injected with CFA and PBS
 - 3 weeks later a boost injection of 10 μg of protein in with incomplete Freund's adjuvant.

VACCINATION PROTOCOL

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- 15 Before challenge at d62, sera was collected at d61 to analyze the antibody response in the vaccinated animals.
 - WB analysis of sera from immunized mice were performed to detect the antibody response to the recombinant proteine used for immunization as described above.
 - An ELISA assay was set up to measure antibody titer in vaccinated animals:
- Each recombinant protein was coated on a 96-well plates with (200 ng/100 μ l coating buffer), plates are saturat with 3%BSA in PBS.
 - Twofold serial dilution of sera were made in PBS 1X/1% BSA from 1:500, to 1: 1024000 and incubated on the plate, antiboby binding was reavealed using a rabbit Anti-mouse IgG conjugated with Peroxydase and OPD(o-phenylenediamine) chromogen substrate.
 - Read the OD_{495} with Sanofi Diagnostics Pasteur PR2100 $\!^{\tiny{\textcircled{\scriptsize 8}}}$

• Results:

Table 1. Sera titer against recombinant protein by ELISA

SEQ ID	serum1	serum 2	serum 3	serum 4	Control	recombinant protein
2	128	64	128	512	<0,5	
140	>64	>64	>64	>64	<0,5	+
31	>64	>64	>64	>64	<0,5	+
49	>64	>64	>64	>64	<0,5	+
51	>64	>64	>64	>64	<0,5	+
25	>64	>64	>64	>64	<0,5	+
7	16	8	>64	<0,5	<0,5	+
19	>64	>64	>64	>64	0,5	+
3	>64	>64	>64	>64	<0,5_	+
26 .	512	128	64	256	<0,5	+
18	>64	>64	>64	>64	0,5	+
32	>64	>64	>64	>64	0,5	+
53	>64	>64	>64	>64	0,5	+
587	>64	16	32	32	<0,5	+
11	>64	32	32	64	<0,5	+
36	512	256	512	256	<0,5	+
10	32	128	256	128	0,5	+
47	512	512	512	512	0,5	+
20	1024	256	256	512	<0,5	+
17	1024	512	128	512	<0,5	+

 To assess the ability of sera to recognize the native antigen expressed by the bacteria, western blot was also performed on whole bacteria lysat.

10 To this end, bacteria were grown in LB medium supplemented or not with iron chelator until OD600=0.5-0.6 and pelleted by centrifugation 5 minutes at 10000 rpm. The pellet was lysed by resuspension in 1X loading buffer containing SDS and heated 5 min at 95°C before migration on the gel.Western blot assay was then performed with sera from controls and vaccinated animals.

Results in table 2 shows the results obtained with Sera from vaccinated mice against recombinant protein and against *E.coli* lysat.

5 Table 2: reactivity in Western Blot of sera from mice vaccinated with polypeptides encoded by the different ORFs

SEQ ID N°	whole cell lysate	recombinant protein
2	+	+
140	+	+
26	+	+

• Protection assay, end point: mortality

At d62, 20 vaccinated and 10 control mice were challenged with an E.coli virulent strain belonging to B2 group at a dose equal to the LD 50 (5.10 5 cfu/mice) by intraperitoneal injection. Mortality is recorded at 48h, results in Table 3 are expressed as a percentage of protection representing the difference of survival in vaccinated versus control mice goups.

20 Table 3: Protection obtained in mice challenged after immunization with proteines encoded by the corresponding ORFs.

SEQ ID N°	% protection
2	52
26	66
36	46
10	30
47	60
20	25

- Protection assay, end point: bacteremia
- 30 At d62, 10 vaccinated and 5 control mice were challenged with an Ecoli virulent strain belonging to B2 group at a dose equal to the 1/5 of the LD 50 (1.10⁵ cfu/mice) by intraperitoneal

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injection.With this infectious dose the mice survived the infection at d48. At 48h blood was collected for each mice in presence of heparin .To assess bacteremia , the blood was plated on LB media and colonies count measured after overnight culture.

Example 2: Distribution of the DNA sequence of ORFs specific for B2/D group of E.coli in clinical isolates.

10 To make a DNA arrays membrane specific for B2/D group of *E.coli*, DNA corresponding to ORFs that were identified as specific for B2/D core genome of *E.coli* was amplified by PCR and spotted on nylon membrane using standard methods to those skilled in the art.

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Chromosomal DNA from 30 *E.coli* clinical isolate strains (of which 23 were from pathological conditions and 6 isolated from human normal flora), was prepared and radiolabelled with 33P.

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DNA from these clinical isolates was then hybridized to the B2/D specific DNA array, the results were read by a phosphoimager and spots reactivity was analyzed with an image analysis software. If hybridization gave a positive signal for a particular ORF, this ORf is considered to be present in the genome of the isolate. Quality control of the array is the hybridization of a probe DNA from a reference strain of *E.coli* as shown in figure 2, which represents a picture of the DNA array after hybridization with the genomic DNA from a B2/D reference strain.

The details of the method used for these experiments has been described previously in Tinsley et al. Methods Enzymol. 2002, 358; 188-207.

5 Results presented in Table 4 are expressed as the frequency of each ORF detection in the three different group A, B and D of *E.coli* strains.

10 Table 4 :Presence of Orfs encoding antigens in *E.coli* clinical isolate genomes

	Clinical isolate groups		
Frequency of positive signal %	A	D	B2
SEQ ID N°	N=6	n=5	n=18
86	17	20	100
119	0	80	100
137	0	0	100
77	0	100	94
78	0	100	100
79	0	100	100
80	0	0	100
84	0	0	100
82	0	0	100
88	0	0	100
83	0	0	94
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76 0 0 56	71	50	100	
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	67.	0	0	50

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158	17	100	89
107	17	0	78
72	50	100	44
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148	0	0	6
	(

Example 3: Vaccines compositions intended for prevention of any form of infection by ExPEC.

5 The polypeptide coded by a sequence comprising SEQ ID $N^{\circ}28$ is conjugated with a toxin and added to a physiologically inert vehicle.

This conjugated peptide is optionnally added to a childhood 10 vaccine.

The composition is sterilized and can be injected parenterally, subcutaneously or intramuscularly.

15 Said composition can also be sprayed onto mucosa with the aid of a spray.

CLAIMS

1. The isolated polypeptides having SEQ ID N° 14, 15, 17, 21, 22, 23, 28, 29, 30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52 to 55, 58, 60, 63, 133-138.

- 2- Isolated antigenic polypeptides according to claim 1 obtainable by a process comprising the steps of :
- a- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria,
 - b- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates,
 - c- purifying the polypeptides identified in step a, which are found in step b to be conserved in B2/D isolates,
 - d- testing the polypeptides for immunogenicity using animals models.
- 3. Isolated polynucleotides, coding for a polypeptide 20 according to claim 1 or 2, according to the universal genetic code.
 - 4. Isolated polynucleotides according to claim 3, having sequences selected in the group comprising SEQ ID N° 80, 81, 83, 87-89, 94-96, 98, 102, 104, 105, 107-110, 112, 115, 116, 118, 119, 126, 127, 130, 132, 135, 146-151.
 - 5. An expression vector comprising at least an isolated polynucleotide according to claim 3 or 4.
 - 6. A host cell comprising an expression vector according to claim 5.

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7. A process for isolating and identifying antigenic polypeptides, useful as vaccines comprising the steps of:

a- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria,

- b- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates.
- c- purifying the polypeptides identified in step a, which are found in step b to be conserved in B2/D isolates,
- 10 d- testing the polypeptides for immunogenicity using animals models.

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- 8. The process of claim 7, comprising the use of infected adult animals, eventually immunodepressed, and of infant animals as models for neonatal infections.
 - 9. The use of at least one polypeptide or fragment of these polypeptides selected in the group comprising SEQ ID $N^{\circ}1$ to SEQ ID $N^{\circ}66$ (except SEQ ID $N^{\circ}8$), or 133-145 as antigens and the homologous sequences.
 - 10. A vaccine composition specific to *E. coli* extraintestinal infections, comprising an effective amount of at
 least one antigenic polypeptide such as selected by the
 process of claim 7, or according to claim 9, alone or in
 combination, particularly at least one polypeptide having a
 sequence selected in the group comprising SEQ ID N°1 to SEQ ID
 N°66, or 133-145, except SEQ ID N°8 and the homologous
 sequences, with a carrier.

11. The vaccine composition of claim 10 for preventing urinary system infections, pyelonephritis, sepsis, bacteremia, neonatal meningitidis.

12. The vaccine composition of claim 10 or 11, adapted to specific indication in combination with components directed against other bacteria, such as *S.aureus* or group B *Streptococcus*. Or other bacteria implicated in systemic infections.

- 13. Antibodies or fragments thereof directed against a polypeptide such as used according to claim 9.
- 10 14. Monoclonal antibodies against epitopes of polypeptide and there use as pharmaceutical compound for treatment or prevention of severe infection due to Expec in neonates and patients at risk for such infections.
- 15. A method for detecting the presence or absence of undesirable extra-intestinal *E. coli*, and/or for the diagnosis of an extra-intestinal *E. coli* infection, comprising the use of at least one polypeptide such as defined in claim 1 or 2 or a polynucleotide according to claim 3 or 4, or an antibody to claim 13 or 14, said polypeptide(s) being optionally in combination with anyone of the polypeptides having SEQ ID N°1-66 to 133-145.
- 16. Pharmaceutical composition for alleviating and/or preventing and/or treating an undesirable growth of *E. coli* comprising an effective amount of at least one polypeptide according to claim 9, in combination with a pharmaceutically acceptable carrier.

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FIGURE 1

buffer pH 5,9 buffer pH 4,5

PM E1 E2 E3 E1 E2 E3 E4

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FIGURE 2

SUBSTITUTE SHEET (RULE 26)

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Pro Arg Gly Tyr Ile Glu Gly Gly Val Ser Ser Arg Asp Ser Tyr Arg 165 170 175

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- Gln His Tyr Ser Arg Thr Phe Pro Ser Gly Ser Leu Ile Val Asn Met 305 310 315 320
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- Gly Asp Ala Arg Thr Val Asp Met Val Phe Gly Leu Tyr Arg Gln Asn 340 345 350
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Gln Phe Ser Ile Pro Val Arg Thr Glu Leu Glu Phe Tyr Ala Arg Gly 85 90 95

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Thr Val Val Leu Asp Asn Ala Tyr Thr Ser Asp Leu Ile Ala Ala Asn 50 55 60

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Asp Gly Leu Asp Leu Phe Thr Gly Val Thr Met Thr Tyr Thr Asp 1070 1075 1080 Ser His Ala Gly Ser Asp Ala Phe Ser Gly Glu Thr Lys Ser Val 1085 1090 Gly Ala Gly Leu Tyr Ala Ser Ala Met Phe Glu Ser Gly Ala Tyr 1105 Ile Asp Leu Ile Gly Lys Tyr Val His His Asp Asn Glu Tyr Thr 1115 1120 Ala Thr Phe Ala Gly Leu Gly Thr Arg Asp Tyr Ser Ser His Ser 1135 1140 Trp Tyr Ala Gly Ala Glu Val Gly Tyr Arg Tyr His Val Thr Asp 1145 1150 Ser Ala Trp Ile Glu Pro Gln Ala Glu Leu Val Tyr Gly Ala Val 1165 Ser Gly Lys Gln Phe Ser Trp Lys Asp Gln Gly Met Asn Leu Thr 1180 Met Lys Asp Lys Asp Phe Asn Pro Leu Ile Gly Arg Thr Gly Val 1195 1200 Asp Val Gly Lys Ser Phe Ser Gly Lys Asp Trp Lys Val Thr Ala 1205 Arg Ala Gly Leu Gly Tyr Gln Phe Asp Leu Phe Ala Asn Gly Glu 1225 , Thr Val Leu Arg Asp Ala Ser Gly Glu Lys Arg Ile Lys Gly Glu 1240 Lys Asp Gly Arg Met Leu Met Asn Val Gly Leu Asn Ala Glu Ile 1260 Arg Asp Asn Leu Arg Phe Gly Leu Glu Phe Glu Lys Ser Ala Phe 1265 1270 1275

Gly Lys Tyr Asn Val Asp Asn Ala Ile Asn Ala Asn Phe Arg Tyr 1285

Ser Phe 1295

<210> 6

<211> 142 <212> PRT <213> Escherichia coli

Met Ile Asn Ile Pro Ser Pro Thr Ala Val Val Met Ala Leu Val Ala 5

Ile Ser Thr Leu Pro Ser Pro Ser Arg Val Lys Leu Met Pro Tyr Pro 20 25

Pro Arg Ala His Asn Thr Thr Gly Leu Leu Pro Val Arg Glu Ile Cys 35 40

Phe Pro His His Gly Asp Asp Gly Arg Asn Ser Ile Glu Pro Ser Ile

Ser Arg Ala Ala His Thr Asp Arg Leu Arg Phe Val Cys Met Thr Arg 75

Thr Gly Ser Thr Thr Ser Arg Pro Phe Cys Pro Ile Pro Arg Ser Pro 90 95

Ala Leu Asn Ala Ser Gly Gln Gln Asp Ser Gly Phe Trp Gly Val Ser 100 105 110

Ser Ile Pro Gly Asp Ile Leu Met Phe Gln Leu His Val Leu Ile Val 120

Phe Ile Cys Lys Ile Asn Leu Ser Asp Asn Asn Ile Ser Tyr

<210> 7

<211> 318 <212> PRT <213> Escherichia coli <400> 7

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10,00

- Met Tyr Ala Arg Glu Tyr Arg Ser Thr Arg Pro His Lys Ala Ile Phe 1 5 10 15
- Phe His Leu Ser Cys Leu Thr Leu Ile Cys Ser Ala Gln Val Tyr Ala
 20 25 30
- Lys Pro Asp Met Arg Pro Leu Gly Pro Asn Ile Ala Asp Lys Gly Ser 35 40 45
- Val Phe Tyr His Phe Ser Ala Thr Ser Phe Asp Ser Val Asp Gly Thr 50 55 60
- Arg His Tyr Arg Val Trp Thr Ala Val Pro Asn Thr Thr Ala Pro Ala 65 70 75 80
- Ser Gly Tyr Pro Ile Leu Tyr Met Leu Asp Gly Asn Ala Val Met Asp 85 90 95
- Arg Leu Asp Glu Leu Leu Lys Gln Leu Ser Glu Lys Thr Pro Pro 100 100 110
- Val Ile Val Ala Val Gly Tyr Gln Thr Asn Leu Pro Phe Asp Leu Asn 115 120 125
- Ser Arg Ala Tyr Asp Tyr Thr Pro Ala Ala Glu Ser Arg Lys Thr Asp 130 135 140
- Leu His Ser Gly Arg Phe Ser Arg Lys Ser Gly Gly Ser Asn Asn Phe 145 150 155 160
- Arg Gln Leu Leu Glu Thr Arg Ile Ala Pro Lys Val Glu Gln Gly Leu 165 170 175
- Asn Ile Asp Arg Gln Arg Arg Gly Leu Trp Gly His Ser Tyr Gly Gly 180 185 190
- Leu Phe Val Leu Asp Ser Trp Leu Ser Ser Ser Tyr Phe Arg Ser Tyr 195 200 205
- Tyr Ser Ala Ser Pro Ser Leu Gly Arg Gly Tyr Asp Ala Leu Leu Ser 210 215 220
- Arg Val Thr Ala Val Glu Pro Leu Gln Phe Cys Thr Lys His Leu Ala

225 230 235 240

Ile Met Glu Gly Ser Ala Thr Gln Gly Asp Asn Arg Glu Thr His Ala
245 250 255

Val Gly Val Leu Ser Lys Ile His Thr Thr Leu Thr Ile Leu Lys Asp
260 265 270

Lys Gly Val Asn Ala Val Phe Trp Asp Phe Pro Asn Leu Gly His Gly 275 280 285

Pro Met Phe Asn Ala Ser Phe Arg Gln Ala Leu Leu Asp Ile Ser Gly 290 295 300

Glu Asn Ala Asn Tyr Thr Ala Gly Cys His Glu Leu Ser His 305 310 315

<210> 8

<211> 725

<212> PRT

<213> Escherichia coli

<400> 8

Met Arg Ile Asn Lys Ile Leu Trp Ser Leu Thr Val Leu Leu Val Gly

1 10 15

Leu Asn Ser Gln Val Ser Val Ala Lys Tyr Ser Asp Asp Asn Asp 20 25 30

Glu Thr Leu Val Val Glu Ala Thr Ala Glu Gln Val Leu Lys Gln Gln 35 40 45

Pro Gly Val Ser Val Ile Thr Ser Glu Asp Ile Lys Lys Thr Pro Pro

Val Asn Asp Leu Ser Asp Ile Ile Arg Lys Met Pro Gly Val Asn Leu
65 70 75

Thr Gly Asn Ser Ala Ser Gly Thr Arg Gly Asn Asn Arg Gln Ile Asp

Ile Arg Gly Met Gly Pro Glu Asn Thr Leu Ile Leu Ile Asp Gly Val

- Pro Val Thr Ser Arg Asn Ser Val Arg Tyr Ser Trp Arg Gly Glu Arg
- Asp Thr Arg Gly Asp Thr Asn Trp Val Pro Pro Glu Gln Val Glu Arg
- Ile Glu Val Ile Arg Gly Pro Ala Ala Ala Arg Tyr Gly Ser Gly Ala 145 150 155 160
- Ala Gly Gly Val Val Asn Ile Ile Thr Lys Arg Pro Thr Asn Asp Trp
 165 170 175
- His Gly Ser Leu Ser Leu Tyr Thr Asn Gln Pro Glu Ser Ser Glu Glu 180 185 190
- Gly Ala Thr Arg Arg Ala Asn Phe Ser Leu Ser Gly Pro Leu Ala Gly 195 200 205
- Asp Ala Leu Thr Thr Arg Leu Tyr Gly Asn Leu Asn Lys Thr Asp Ala 210 215 220
- Asp Ser Trp Asp Ile Asn Ser Pro Val Gly Thr Lys Asn Ala Ala Gly 225 230 235 240
- His Glu Gly Val Arg Asn Lys Asp Ile Asn Gly Val Val Ser Trp Lys 245 250 255
- Leu Asn Pro Gln Gln Ile Leu Asp Phe Glu Val Gly Tyr Ser Arg Gln 260 265 270
- Gly Asn Ile Tyr Ala Gly Asp Thr Gln Asn Ser Ser Ser Ser Ala Val 275 280 285
- Thr Glu Ser Leu Ala Lys Ser Gly Lys Glu Thr Asn Arg Leu Tyr Arg 290 295 300
- Gln Asn Tyr Gly Ile Thr His Asn Gly Ile Trp Asp Trp Gly Gln Ser 305 310 315 320
- Arg Phe Gly Val Tyr Tyr Glu Lys Thr Asn Asn Thr Arg Met Asn Glu 325 330 335
- Gly Leu Ser Gly Gly Gly Glu Gly Arg Ile Leu Ala Gly Glu Lys Phe

340 345 350

Thr Thr Asn Arg Leu Ser Ser Trp Arg Thr Ser Gly Glu Leu Asn Ile 355 360 365

Pro Leu Asn Val Met Val Asp Gln Thr Leu Thr Val Gly Ala Glu Trp 370 375

Asn Arg Asp Lys Leu Asp Asp Pro Ser Ser Thr Ser Leu Thr Val Asn 385 390 395 400

Asp Arg Asp Ile Ser Gly Ile Ser Gly Ser Ala Ala Asp Arg Ser Ser 405 410 415

Lys Asn His Ser Gln Ile Ser Ala Leu Tyr Ile Glu Asp Asn Ile Glu 420 425 430

Pro Val Pro Gly Thr Asn Ile Ile Pro Gly Leu Arg Phe Asp Tyr Leu 435 440 445

Ser Asp Ser Gly Gly Asn Phe Ser Pro Ser Leu Asn Leu Ser Gln Glu 450 455 460

Leu Gly Asp Tyr Phe Lys Val Lys Ala Gly Val Ala Arg Thr Phe Lys 465 470 475 480

Ala Pro Asn Leu Tyr Gln Ser Ser Glu Gly Tyr Leu Leu Tyr Ser Lys 485 490 495

Gly Asn Gly Cys Pro Lys Asp Ile Thr Ser Gly Gly Cys Tyr Leu Ile 500 510

Gly Asn Lys Asp Leu Asp Pro Glu Ile Ser Val Asn Lys Glu Ile Gly 515 520 525

Leu Glu Phe Thr Trp Glu Asp Tyr His Ala Ser Val Thr Tyr Phe Arg 530 535 540

Asn Asp Tyr Gln Asn Lys Ile Val Ala Gly Asp Asn Val Ile Gly Gln 545 550 555 560

Thr Ala Ser Gly Ala Tyr Ile Leu Lys Trp Gln Asn Gly Gly Lys Ala
565 570 575

Leu Val Asp Gly Ile Glu Ala Ser Met Ser Phe Pro Leu Val Lys Glu 580 585 590

Arg Leu Asn Trp Asn Thr Asn Ala Thr Trp Met Ile Thr Ser Glu Gln 595 600 605

Lys Asp Thr Gly Asn Pro Leu Ser Val Ile Pro Lys Tyr Thr Ile Asn 610 615 620

Asn Ser Leu Asn Trp Thr Ile Thr Gln Ala Phe Ser Ala Ser Phe Asn 625 630 635 640

Trp Thr Leu Tyr Gly Arg Gln Lys Pro Arg Thr His Ala Glu Thr Arg 645 650 655

Ser Glu Asp Thr Gly Gly Leu Ser Gly Lys Glu Leu Gly Ala Tyr Ser

Leu Val Gly Thr Asn Phe Asn Tyr Asp Ile Asn Lys Asn Leu Arg Leu 675 680 685

Asn Val Gly Val Ser Asn Ile Leu Asn Lys Gln Ile Phe Arg Ser Ser 690 695 700

Glu Gly Ala Asn Thr Tyr Asn Glu Pro Gly Arg Ala Tyr Tyr Ala Gly
705 710 715 720

Val Thr Ala Ser Phe 725

<210> 9

<211> 1014

<212> PRT

<213> Escherichia coli

<400> 9

Met Gly Asn Gln Trp Gln Gln Lys Tyr Leu Leu Glu Tyr Asn Glu Leu 1 5 10 15

Val Ser Asn Phe Pro Ser Pro Glu Arg Val Val Ser Asp Tyr Ile Lys
20 25 30

Asn Cys Phe Lys Thr Asp Leu Pro Trp Phe Ser Arg Ile Asp Pro Asp

 $\sum_{i=1}^{n} (i - 1)^{n}$

35

40

45

Asn Ala Tyr Phe Ile Cys Phe Ser Gln Asn Arg Ser Asn Ser Arg Ser 50 55 60

Tyr Thr Gly Trp Asp His Leu Gly Lys Tyr Lys Thr Glu Val Leu Thr 65 70 75 80

Leu Thr Gln Ala Ala Leu Ile Asn Ile Gly Tyr Arg Phe Asp Val Phe 85 90 95

Asp Asp Ala Asn Ser Ser Thr Gly Ile Tyr Lys Thr Lys Ser Ala Asp 100 105 110

Val Phe Asn Glu Glu Asn Glu Glu Lys Met Leu Pro Ser Glu Tyr Leu 115 120 125

Ser Asp Tyr Trp Ser Lys Tyr Tyr Asp Lys Phe Lys Leu Leu Lys 145 150 150

Asn Tyr Tyr Ile Ser Ser Ala Leu Tyr Leu Tyr Lys Asn Gly Glu Leu 165 170 175

Asp Glu Arg Glu Tyr Asn Phe Ser Met Asn Ala Leu Asn Arg Ser Asp 180 185 190

Asn Ile Ser Leu Leu Phe Phe Asp Ile Tyr Gly Tyr Tyr Ala Ser Asp 195 200 205

Ile Phe Val Ala Lys Asn Asn Asp: Lys Val Met Leu Phe Ile Pro Gly 210 215 220

Ala Lys Lys Pro Phe Leu Phe Lys Lys Asn Ile Ala Asp Leu Arg Leu 225 230 230 235 240

Thr Leu Lys Glu Leu Ile Lys Asp Ser Asp Asn Lys Gln Leu Leu Ser 245 250 255

Gln His Phe Ser Leu Tyr Ser Arg Gln Asp Gly Val Ser Tyr Ala Gly 260 265 270

- Val Asn Ser Val Leu His Ala Ile Glu Asn Asp Gly Asn Phe Asn Glu 275 280 285
- Ser Tyr Phe Leu Tyr Ser Asn Lys Thr Leu Ser Asn Lys Asp Val Phe 290 295 300
- Asp Ala Ile Ala Ile Ser Val Lys Lys Arg Ser Phe Ser Asp Gly Asp 305 310 315 320
- Ile Val Ile Lys Ser Asn Ser Glu Ala Gln Arg Asp Tyr Ala Leu Thr 325 330 335
- Ile Leu Gln Thr Ile Leu Ser Met Thr Pro Ile Phe Asp Ile Val Val 340 345 350
- Pro Glu Val Ser Val Pro Leu Gly Leu Gly Ile Ile Thr Ser Ser Met 355 360 365
- Gly Ile Ser Phe Asp Gln Leu Ile Asn Gly Asp Thr Tyr Glu Glu Arg 370 375 380
- Arg Ser Ala Ile Pro Gly Leu Ala Thr Asn Ala Val Leu Leu Gly Leu 385 390 395 400
- Ser Phe Ala Ile Pro Leu Leu Ile Ser Lys Ala Gly Ile Asn Gln Glu 405 410 415
- Val Leu Ser Ser Val Ile Asn Asn Glu Gly Arg Thr Leu Asn Glu Thr
 420 425 430
- Asn Ile Asp Ile Phe Leu Lys Glu Tyr Gly Ile Ala Glu Asp Ser Ile 435 440 , 445
- Ser Ser Thr Asn Leu Leu Asp Val Lys Leu Lys Ser Ser Gly Gln His 450 455 460
- Val Asn Ile Val Lys Leu Ser Asp Glu Asp Asn Gln Ile Val Ala Val 465 470 475 480
- Lys Gly Ser Ser Leu Ser Gly Ile Tyr Tyr Glu Val Asp Ile Glu Thr

(:: :

 $\{\hat{x}_i\}_{i=1}^{n}$

- Gly Tyr Glu Ile Leu Ser Arg Arg Ile Tyr Arg Thr Glu Tyr Asn Asn 500 505 510
- Glu Ile Leu Trp Thr Arg Gly Gly Gly Leu Lys Gly Gly Gln Pro Phe 515 520 525
- Asp Phe Glu Ser Leu Asn Ile Pro Val Phe Phe Lys Asp Glu Pro Tyr 530 540
- Ser Ala Val Thr Gly Ser Pro Leu Ser Phe Ile Asn Asp Asp Ser Ser 545 550 555 560
- Leu Leu Tyr Pro Asp Thr Asn Pro Lys Leu Pro Gln Pro Thr Ser Glu 565 570 575
- Met Asp Ile Val Asn Tyr Val Lys Gly Ser Gly Ser Phe Gly Asp Arg 580 585 590
- Phe Val Thr Leu Met Arg Gly Ala Thr Glu Glu Glu Ala Trp Asn Ile 595 600 605
- Ala Ser Tyr His Thr Ala Gly Gly Ser Thr Glu Glu Leu His Glu Ile 610 615 620
- Leu Leu Gly Gln Gly Pro Gln Ser Ser Leu Gly Phe Thr Glu Tyr Thr 625 630 635 640
- Ser Asn Val Asn Ser Ala Asp Ala Ala Ser Arg Arg His Phe Leu Val 645 650 655
- Val Ile Lys Val His Val Lys Tyr Ile Thr Asn Asn Asn Val Ser Tyr 660 665 670
- Val Asn His Trp Ala Ile Pro Asp Glu Ala Pro Val Glu Val Leu Ala 675 680 685
- Val Val Asp Arg Arg Phe Asn Phe Pro Glu Pro Ser Thr Pro Pro Asp 690 695 700
- Ile Ser Thr Ile Arg Lys Leu Leu Ser Leu Arg Tyr Phe Lys Glu Ser 705 710 715 720

- Ile Glu Ser Thr Ser Lys Ser Asn Phe Gln Lys Leu Ser Arg Gly Asn 725 730 735
- Ile Asp Val Leu Lys Gly Arg Gly Ser Ile Ser Ser Thr Arg Gln Arg
 740 745 750
- Ala Ile Tyr Pro Tyr Phe Glu Ala Ala Asn Ala Asp Glu Gln Gln Pro 755 760 765
- Leu Phe Phe Tyr Ile Lys Lys Asp Arg Phe Asp Asn His Gly Tyr Asp 770 780
- Gln Tyr Phe Tyr Asp Asn Thr Val Gly Leu Asn Gly Ile Pro Thr Leu 785 790 795 800
- Asn Thr Tyr Thr Gly Glu Ile Pro Ser Asp Ser Ser Ser Leu Gly Ser 805 810 815
- Thr Tyr Trp Lys Lys Tyr Asn Leu Thr Asn Glu Thr Ser Ile Ile Arg 820 825 830
- Val Ser Asn Ser Ala Arg Gly Ala Asn Gly Ile Lys Ile Ala Leu Glu 835 840 845
- Glu Val Gln Glu Gly Lys Pro Val Ile Ile Thr Ser Gly Asn Leu Ser 850 855 860
- Gly Cys Thr Thr Ile Val Ala Arg Lys Glu Gly Tyr Ile Tyr Lys Val 865 870 875 880
- His Thr Gly Thr Thr Lys Ser Leu Ala Gly Phe Thr Ser Thr Thr Gly 885 890 895
- Val Lys Lys Ala Val Glu Val Leu Glu Leu Leu Thr Lys Glu Pro Ile 900 905 910
- Pro Arg Val Glu Gly Ile Met Ser Asn Asp Phe Leu Val Asp Tyr Leu 915 920 925
- Ser Glu Asn Phe Glu Asp Ser Leu Ile Thr Tyr Ser Ser Ser Glu Lys 930 935 940
- Lys Pro Asp Ser Gln Ile Thr Ile Ile Arg Asp Asn Val Ser Val Phe

23

945 950 955 960

Pro Tyr Phe Leu Asp Asn Ile Pro Glu His Gly Phe Gly Thr Ser Ala 965 970

Thr Val Leu Val Arg Val Asp Gly Asn Val Val Val Arg Ser Leu Ser 985

Glu Ser Tyr Ser Leu Asn Ala Asp Ala Ser Glu Ile Ser Val Leu Lys 1000

Val Phe Ser Lys Lys Phe 1010

<210> 10

<211> 454

<212> PRT

<213> Escherichia coli <400> 10

Met Val Asp Met Ile Asn Glu Ser Ala Arg Gln Thr Pro Val Ile Ala

Gln Thr Asp Val Leu Val Ile Gly Gly Gly Pro Ala Gly Leu Ser Ala 20 25

Ala Ile Ala Ala Gly Arg Leu Gly Ala Arg Thr Met Ile Val Glu Arg 35 40

Tyr Gly Ser Leu Gly Gly Val Leu Thr Gln Val Gly Val Glu Ser Phe 50 55 60

Ala Trp Tyr Arg His Pro Gly Thr Glu Asp Cys Glu Gly Ile Cys Arg 70 75

Glu Tyr Glu Gly Arg Ala Arg Ala Leu Gly Phe Thr Arg Pro Glu Pro 85 90

Gln Ser Ile Ser Glu Val Ile Asp Thr Glu Gly Phe Lys Val Val Ala 100

Asp Gln Met Ile Thr Glu Ser Gly Val Glu Pro Leu Tyr His Ser Trp 115 120

(P.)

- Val Val Asp Val Ile Lys Asp Gly Asp Thr Leu Cys Gly Val Ile Val 130 135 140
- Cys Thr Gly Asp Ala Asp Ile Ala Ala Arg Ala Gly Ala Pro Trp Thr
 165 170 175
- Lys Arg Ser Lys Asp Gln Leu Met Gly Val Thr Val Met Phe Ser Cys
 180 185 190
- Ala Gly Val Asp Val Ala Arg Phe Asn Arg Phe Val Ala Glu Glu Leu 195 200 205
- Lys Pro Thr Tyr Ala Asp Trp Gly Lys Asn Trp Thr Ile Gln Thr Thr 210 215 220
- Gly Lys Glu Asp Pro Met Phe Ser Pro Tyr Met Glu Asp Ile Phe Thr 225 235 235
- Arg Ala Gln Gln Asp Gly Val Ile Pro Gly Asp Ala Gln Ala Ile Ala 245 250 255
- Gly Thr Trp Ser Thr Phe Ser Glu Ser Gly Glu Ala Phe Gln Met Asn 260 265 270
- Met Val Tyr Ala Phe Gly Phe Asp Cys Thr Asp Val Phe Asp Leu Thr 275 280 285
- Lys Ala Glu Ile Ala Gly Arg Gln Gln Ala Leu Trp Ala Ile Asp Ala 290 295 300
- Leu Arg His Tyr Val Pro Gly Phe Glu Asn Val Arg Leu Arg Asn Phe 305 310 315 320
- Gly Ala Thr Leu Gly Thr Arg Glu Ser Arg Leu Ile Glu Gly Glu Ile 325 330 335
- Arg Ile Ala Asp Asp Tyr Val Leu Asn Gln Gly Arg Cys Ser Asp Ser 340 345 350
- Val Gly Ile Phe Pro Glu Phe Ile Asp Gly Ser Gly Tyr Leu Ile Leu

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355

360

365

Pro Thr Thr Gly Arg Phe Phe Gln Ile Pro Tyr Gly Cys Leu Val Pro 370 380

Gln Lys Val Glu Asn Leu Leu Val Ala Gly Arg Cys Ile Ser Ala Gly 385 390 395 400

Val Val Ala His Thr Ser Met Arg Asn Met Met Cys Cys Ala Val Thr 405 410 415

Gly Glu Ala Ala Gly Thr Ala Ala Val Val Ser Leu Gln Gln Asn Cys 420 425 430

Thr Val Arg Gln Val Ala Ile Pro Asp Leu Gln Asn Thr Leu Gln Gln 435

Gln Gly Val Arg Leu Ala 450

<210> 11

<211> 253

<212> PRT

<213> Escherichia coli

<400> 11

Met Ser Ala Lys Arg Arg Leu Leu Ile Ala Cys Thr Leu Ile Thr Ala 1 5 10 10 15

Ile Tyr His Phe Pro Ala Tyr Ser Ser Leu Glu Tyr Lys Gly Thr Phe 20 25 30

Gly Ser Ile Asn Ala Gly Tyr Ala Asp Trp Asn Ser Gly Phe Val Asn 35 40 45

Thr His Arg Gly Glu Val Trp Lys Val Thr Ala Asp Phe Gly Val Asn 50 55 60

Phe Lys Glu Ala Glu Phe Tyr Ser Phe Tyr Glu Ser Asn Val Leu Asn 65 70 75 80

His Ala Val Ala Gly Arg Asn His Thr Val Ser Ala Met Thr His Val 85 90 95

Arg Leu Phe Asp Ser Asp Met Thr Phe Phe Gly Lys Ile Tyr Gly Gln

Trp Asp Asn Ser Trp Gly Asp Asp Leu Asp Met Phe Tyr Gly Phe Gly 115

Tyr Leu Gly Trp Asn Gly Glu Trp Gly Phe Phe Lys Pro Tyr Ile Gly 130 135 140

Leu His Asn Gln Ser Gly Asp Tyr Val Ser Ala Lys Tyr Gly Gln Thr
150 155

Asn Gly Trp Asn Gly Tyr Val Val Gly Trp Thr Ala Val Leu Pro Phe 165 170 175

Thr Leu Phe Asp Glu Lys Phe Val Leu Ser Asn Trp Asn Glu Ile Glu 180 185 190

Leu Asp Arg Asn Asp Ala Tyr Thr Glu Gln Gln Phe Gly Arg Asn Gly 195 200 205

Leu Asn Gly Gly Leu Thr Ile Ala Trp Lys Phe Tyr Pro Arg Trp Lys 210 215 220

Ala Ser Val Thr Trp Arg Tyr Phe Asp Asn Lys Leu Gly Tyr Asp Gly 235 235 240

Phe Gly Asp Gln Met Ile Tyr Met Leu Gly Tyr Asp Phe 245

<210> 12

<211> 492

<212> PRT

<213> Escherichia coli

<400> 12

Met Ala Ser Leu Ile Gly Leu Ala Val Cys Thr Gly Asn Ala Phe Ser 1 5 10 15

Pro Ala Leu Ala Ala Glu Ala Lys Gln Pro Asn Leu Val Ile Ile Met 20 25 30

Ala Asp Asp Leu Gly Tyr Gly Asp Leu Ala Thr Tyr Gly His Gln Ile 35 40 45

- Val Lys Thr Pro Asn Ile Asp Arg Leu Ala Gln Glu Gly Val Lys Phe 50 55 60
- Thr Asp Tyr Tyr Ala Pro Ala Pro Leu Ser Ser Pro Ser Arg Ala Gly 70 75 80
- Leu Leu Thr Gly Arg Met Pro Phe Arg Thr Gly Ile Arg Ser Trp Ile 85 90 95
- Pro Ser Gly Lys Asp Val Ala Leu Gly Arg Asn Glu Leu Thr Ile Ala
- Asn Leu Leu Lys Ala Gln Gly Tyr Asp Thr Ala Met Met Gly Lys Leu 115
- His Leu Asn Ala Gly Gly Asp Arg Thr Asp Gln Pro Gln Ala Gln Asp 130 135 140
- Met Gly Phe Asp Tyr Ser Leu Ala Asn Thr Ala Gly Phe Val Thr Asp 145 150 155 160
- Ala Thr Leu Asp Asn Ala Lys Glu Arg Pro Arg Tyr Gly Met Val Tyr
 165 170 175
- Pro Thr Gly Trp Leu Arg Asn Gly Gln Pro Thr Pro Arg Ala Asp Lys
 180 185 190
- Met Ser Gly Glu Tyr Val Ser Ser Glu Val Val Asn Trp Leu Asp Asn 195 200 205
- Lys Lys Asp Ser Lys Pro Phe Phe Leu Tyr Val Ala Phe Thr Glu Val 210 215 220
- His Ser Pro Leu Ala Ser Pro Lys Lys Tyr Leu Asp Met Tyr Ser Gln
 225 230 235 240
- Tyr Met Ser Ala Tyr Gln Lys Gln His Pro Asp Leu Phe Tyr Gly Asp 245 250
- Trp Ala Asp Lys Pro Trp Arg Gly Val Gly Glu Tyr Tyr Ala Asn Ile 260 265 270

באכטטכיטי אויט

- Ser Tyr Leu Asp Ala Gln Val Gly Lys Val Leu Asp Lys Ile Lys Ala 275 280 285
- Met Gly Glu Glu Asp Asn Thr Ile Val Ile Phe Thr Ser Asp Asn Gly 290 295 300
- Pro Val Thr Arg Glu Ala Arg Lys Val Tyr Glu Leu Asn Leu Ala Gly 305 310 315 320
- Glu Thr Asp Gly Leu Arg Gly Arg Lys Asp Asn Leu Trp Glu Gly Gly 325 330 335
- Ile Arg Val Pro Ala Ile Ile Lys Tyr Gly Lys His Leu Pro Gln Gly 340 345 350
- Met Val Ser Asp Thr Pro Val Tyr Gly Leu Asp Trp Met Pro Thr Leu 355 360 365
- Ala Lys Met Met Asn Phe Lys Leu Pro Thr Asp Arg Thr Phe Asp Gly 370 375 380
- Glu Ser Leu Val Pro Val Leu Glu Gln Lys Ala Leu Lys Arg Glu Lys 385 390 395 400
- Pro Leu Ile Phe Gly Ile Asp Met Pro Phe Gln Asp Asp Pro Thr Asp 405 410 415
- Glu Trp Ala Ile Arg Asp Gly Asp Trp Lys Met Ile Ile Asp Arg Asn 420 425 430
- Asn Lys Pro Lys Tyr Leu Tyr Asn Leu Lys Ser Asp Arg Tyr Glu Thr 435 440 445
- Leu Asn Leu Ile Gly Lys Lys Pro Asp Ile Glu Lys Gln Met Tyr Gly 450 455
- Lys Phe Leu Lys Tyr Lys Thr Asp Ile Asp Asn Asp Ser Leu Met Lys 465 470 475 480
- Ala Arg Gly Asp Lys Pro Glu Ala Val Thr Trp Gly 485 490

<210> 13

- <211> 345
- <212> PRT
- <213> Escherichia coli
- <400> 13
- Leu Ile Ser Leu Ser Phe Ile Pro Val Met Ser Ala Leu Pro Gly Pro 1 5 10 15
- Ile Ala Lys Gly Phe Arg Asn Glu Arg Gly Phe Val Thr Thr Ile
 20 25 30
- Cys Ala Met Gly Glu Leu Leu Ala Glu Phe Leu Ser Arg Asn Pro His 35 40 45
- Gln Lys Phe Thr Gln Pro Gly Glu Phe Ile Gly Pro Phe Pro Ser Gly 50 55 60
- Ala Pro Ala Ile Phe Ala Ala Gln Val Ala Lys Leu Ser His Arg Ala 65 70 75 80
- Ile Phe Phe Gly Cys Val Gly Asn Asp Asp Phe Ala Arg Leu Ile Ile 85 90 95
- Glu Arg Leu Arg His Glu Gly Val Ile Thr Asp Gly Ile His Val Met
- Asn Asn Ala Val Thr Gly Thr Ala Phe Val Ser Tyr Gln Asn Pro Gln 115 120 125
- Gln Arg Asp Phe Val Phe Asn Ile Pro Asn Ser Ala Cys Gly Leu Phe 130 140
- Thr Ala Glu His Ile Asp Lys Asp Leu Leu Lys Gln Cys Asn His Leu 145 150 155 160
- His Ile Val Gly Ser Ser Leu Phe Ser Phe Arg Met Ile Asp Val Met 165 170 175
- Arg Lys Ala Ile Thr Thr Ile Lys Ser Ala Gly Gly Thr Val Ser Phe
 180 185 190
- Asp Pro Asn Ile Arg Lys Glu Met Leu Ser Ile Pro Glu Met Ala Gln 195 200 205

Ala Leu Asp Tyr Leu Ile Glu Tyr Thr Asp Ile Phe Ile Pro Ser Glu 210 215 220

Ser Glu Leu Pro Phe Phe Ala Arg His Lys Asn Leu Ser Glu Glu Gln 225 230 235 240

Ile Val Ser Asp Leu Leu His Gly Gly Val Lys His Val Ala Ile Lys 245 250 250

Arg Ala Gln Arg Gly Ala Ser Tyr Tyr Lys Leu Lys Asn Gly Thr Leu 260 265 270

His Ala Gln His Val Ala Gly His Asp Ile Glu Ile Ile Asp Pro Thr 275 280 285

Gly Ala Gly Asp Cys Phe Gly Ala Thr Phe Ile Thr Leu Phe Leu Ser 290 295 300

Gly Phe Pro Ala His Lys Ala Leu Gln Tyr Ala Asn Ala Ser Gly Ala 305 310 315 320

Leu Ala Val Met Arg Gln Gly Pro Met Glu Gly Ile Ser Ser Leu Ala 325 330 335

Asp Ile Glu Asp Phe Leu Gln Gln His 340

<210> 14

<211> 192

<212> PRT

<213> Escherichia coli

<400> 14

Met Tyr Met Pro Gly Lys Gln Met Leu Cys Cys Ile Leu Ile Ser Ile 1 5 , 10 15

Ile Ser Glu Gly Asp Met Lys Ile Phe Ile Ser Leu Phe Leu Phe Ile
20 25 30

Ile Ser Thr Asn Ser Phe Ala Asp Asp Ile Thr His Ala Gly Val Val 35 40 45

Arg Ile Glu Gly Leu Ile Thr Glu Lys Thr Cys Ile Ile Ser Asp Glu 50 55 60

Ser Lys Asn Phe Thr Val Asn Met Pro Asp Val Pro Ser Ser Ser Val 65 70 75 80

Arg Ser Ala Gly Asp Val Thr Glu Lys Val Tyr Phe Ser Ile Thr Leu 85 90 95

Thr Arg Cys Gly Ser Asp Val Gly Asn Ala Tyr Ile Lys Phe Thr Gly
100 105 110

Asn Thr Val Ser Glu Asp Ala Ser Leu Tyr Lys Leu Glu Asp Gly Ser 115 120 125

Val Glu Gly Leu Ala Leu Thr Ile Phe Asp Lys Asn Lys Gly Ser Ile 130 135 140

Ser Asn Asp Val Lys Ser Met Val Phe Ser Leu Thr Ser Ser Val Asp 145 150 155 160

Asn Ile Leu His Phe Phe Ala Ala Tyr Lys Ala Leu Lys Asn Asn Val 165 170 175

Gln Pro Gly Asp Ala Asn Ala Ser Val Ser Phe Ile Val Thr Tyr Asp 180 185 190

<210> 15

<211> 201

<212> PRT

<213> Escherichia coli

<400> 15

Met Ile Lys Phe Arg Leu Tyr Ile Pro Pro Val Ile Leu Gly Phe Val 1 5 10 15

Ile Val Pro Leu Leu Val Trp Pro Thr Val Ile Ala Leu Ala Val Leu 20 25.

Ile Phe Thr Leu Thr Phe Leu Ala Glu Ile Ile Phe Ser Phe Pro Leu 35 40 45

Leu Val Val Arg Ile Ser Leu Gln Glu Leu Gln Leu Glu Leu Leu Val 50 60

Val Tyr Ala Leu Phe Phe Ser Val Met Gly Gly Ile Gly Trp Gln Phe 65 70 75 80

Ser Arg Arg Thr Pro Pro Glu Leu Lys Asn Arg Leu His Cys Trp Leu 85 90 95

Val Phe Ser Pro Val Tyr Phe Trp Leu Ile Leu Ser Asn Phe Ile Leu 100 105 110

Tyr Ile Ser Pro Glu Lys Ser Ala Leu Leu Glu Asn Ile Arg Asn Phe 115 120 125

Phe Leu Thr Phe Val Trp Leu Pro Leu Asn Phe Ser Pro Phe Trp Pro 130 135 140

Gln Pro Trp Thr Asp Phe Val Gly Pro Ile Ser Ala Gln Leu Gly Phe 145 150 155 160

Ala Leu Gly Tyr Tyr Cys Gln Trp Arg Ser Lys Asn Arg Ser His Arg 165 170 175

Lys Lys Trp Gly Asp Trp Val Thr Cys Leu Ser Leu Ala Ile Leu Ala 180 185 190

Leu Gly Pro Leu Phe Asn Tyr Leu Gln
195

<210> 16

<211> 234

<212> PRT

<213> Escherichia coli

<400> 16

Met Lys Phe Asn Leu Ser Asn Leu Ser Ala Val Leu Leu Ala Ser Gly

1 10 15

Met Leu Met Ser Thr Ala Val Thr Ala Ala Pro Gly Asp Ala Thr Gln 20 25 30

Phe Gly Gly Ala Asp Thr Asp Trp Ser Thr Val Asp Tyr Pro Arg Leu 35 40 45

Thr Asp Met Asp Asp Asn Val Asp Ser Met Gly Gly Lys Ile Arg Phe 50 55 60

Thr Gly Arg Val Val Lys Ala Thr Cys Lys Val Ala Thr Asp Ser Lys

33

65 70 75 80

Gln Ile Glu Val Val Leu Pro Val Val Pro Ser Asn Leu Phe Thr Gly
85 90 95

Ile Asp Val Glu Ala Gln Gly Ala Ser Asn Gln Thr Asp Phe Asn Ile
100 105 110

Asn Leu Thr Glu Cys Ser Asn Thr Asp Asp Gln Lys Ile Glu Phe Arg

Phe Thr Gly Thr Ala Asp Ser Ala Asn Lys Thr Leu Ala Asn Glu Val

Glu Gly Ser Thr Asp Ala Asp Asn Ser Gly Asn Ala Gly Ala Thr Gly
145 150 155 160

Val Gly Ile Arg Ile Tyr Ser Lys Gly Thr Thr Asn Asn Gly Leu Ile 165 170 175

Asn Leu Asn Thr Thr Ala Ala Glu Gly Ser Ala Ser Thr Ala Ala Tyr 180 185 190

Thr Ile Pro Gly Asn Ala Thr Thr His Asp Phe Ser Ala Ala Phe Thr 195 200 200

Ala Gly Tyr Ala Gln Asn Gly Ser Thr Val Ala Pro Gly Val Val Lys
210 215 220

Ser Thr Ala Ser Phe Val Val Leu Tyr Glu 225 230

<210> 17

<211> 336

<212> PRT

<213> Escherichia coli

<400> 17

Met Arg Ile His Thr Tyr Trp Tyr Arg Arg Tyr Phe Ile Leu Leu Ile
1 10 15

Ile Ile Phe Ser Asn Val Leu Ser Ser Ile Ala Asn Ala Glu Asp Met 20 25 30

- Gly Arg Glu Arg Ala Tyr Cys Tyr Pro Gly Ser Pro Ser Asn Asn Thr 35 40 45
- Thr Pro Ala Ser Phe Ser Tyr Asn Phe Gly Thr Ile Val Val Ser Asp 50 55 60
- Val Asn Lys Asn Ala Pro Gly Thr Val Leu Pro Ser Gln Ile Trp Lys 65 70 75 80
- Val Gly Thr Tyr Lys Ala Tyr Cys Asn Ser Leu Asp Asp Tyr Glu Ile 85 90 95
- Tyr Phe Ser Ala Val Ser Gly Ile Asp Pro Ser Gly Ala Ser Gly Asp 100 105 110
- His Gln Gly Ser Asp Val Phe Ile Pro Leu Thr His Glu Ile Ser Val
- Ser Thr His Ile Lys Leu Tyr Asn Gln Asn Gly Thr Met Thr Asp Lys 130 135 140
- Ile Val Pro Phe Glu Asn Tyr Asn Thr Asn Tyr Pro Gly Asp Arg Ser 145 150 155 160
- Lys Pro Ser Asn Trp Ala Ser Gly Thr Glu Gly Tyr Ile Lys Ile Arg 165 170 175
- Ile Asp Lys Ile Ile Ser Asp Val Ser Leu Ser Asn Val Leu Leu 180 185 190
- Val Ser Leu Tyr Val Ser Gln Ile Pro Thr Glu His Gly Pro Ile Pro 195 200 205
- Val Phe Asn Ala Tyr Ile Gly Asn Leu Asn Ile Gln Val Pro Gln Gly 210 215 220
- Cys Thr Ile Asn Glu Gly Thr Ser Phe Thr Val Asn Met Pro Asp Val 225 230 235 240
- Trp Ala Ser Glu Leu Ser Arg Ala Gly Ala Gly Ala Lys Pro Ala Gly 245 250 255
- Val Thr Pro Val Ala Thr Thr Ile Pro Ile Asn Cys Thr Asn Lys Asp

()

(***

260

265

270

Thr Asp Ala Val Met Thr Leu Val Phe Asp Gly Asn Ile Ser Ala Thr 275

Arg Asp Thr Asn Gly Lys Gln Ser Ile Ile Gln Ala Gln Asp Asn Pro 290

Asp Val Gly Ile Met Ile Met Asp Ser Gln Gln Asn Ser Val Asp Leu

Asn Ala Leu Ala Thr Ser Val Gly Val Pro Phe Arg Leu Val Glu Asn

<210> 18

<211> 864

<212> PRT

<213> Escherichia coli <400> 18

שאופחחרות. אווח

Met Asn Leu Lys Leu Lys Arg Cys Glu Tyr Trp Met Ala Ala Gln Lys 10

Gln Met Lys Arg Val Val Pro Leu Leu Leu Val Ile Met Pro Ala Cys

Ser Ile Ala Gly Met Arg Phe Asn Pro Ala Phe Leu Ser Gly Asp Thr

Glu Ala Val Ala Asp Leu Ser Arg Phe Glu Lys Gly Met Thr Tyr Leu

Pro Gly Ser Tyr Glu Val Glu Val Trp Val Asn Asp Ser Pro Leu Leu

Ser Arg Thr Val Thr Phe Lys Ala Asp Asp Glu Asn Gln Leu Ile Pro

Cys Leu Ser Leu Ala Asp Leu Leu Ser Leu Gly Ile Asn Lys Asn Ala 100

Leu Pro Glu Gln Ala Leu Ala Ser Ser Glu Asn Ser Cys Leu Asp Leu 120 125

- Arg Ile Trp Phe Pro Asp Val His Tyr Met Pro Glu Leu Asp Ala Gln 130 135 140
- Arg Leu Lys Leu Thr Phe Pro Gln Ala Ile Ile Lys Arg Asp Ala Arg 145 150 155 160
- Gly Tyr Ile Pro Pro Glu Gln Trp Asp Asn Gly Ile Thr Ala Phe Leu 165 170 175
- Leu Asn Tyr Asp Phe Ser Gly Asn Asn Asp Arg Gly Asp Tyr Ser Ser 180 185 190
- Asn Asn Tyr Tyr Leu Asn Leu Arg Ala Gly Ile Asn Ile Gly Ala Trp
 195 200 205
- Arg Phe Arg Asp Tyr Ser Thr Trp Ser Arg Gly Ser Asn Ser Ala Gly 210 215 220
- Lys Leu Glu His Ile Ser Ser Thr Leu Gln Arg Val Ile Ile Pro Phe 225 230 235 240
- Arg Ser Glu Leu Thr Leu Gly Asp Thr Trp Ser Ser Ser Asp Val Phe 245 250 255
- Asp Ser Val Ser Ile Arg Gly Ile Lys Leu Glu Ser Asp Glu Asn Met 260 265 270
- Leu Pro Asp Ser Gln Ser Gly Phe Ala Pro Thr Val Arg Gly Ile Ala 275 280 285
- Lys Ser Arg Ala Gln Val Thr Ile Lys Gln Asn Gly Tyr Val Ile Tyr 290 295 300
- Gln Thr Tyr Met Pro Pro Gly Pro Phe Glu Ile Ser Asp Leu Asn Pro 305 310 315 320
- Thr Ser Ser Ala Gly Asp Leu Glu Val Thr Ile Lys Glu Ser Asp Asn . 325 330 335
- Ser Glu Thr Val Tyr Thr Val Pro Tyr Ala Ala Val Pro Ile Leu Gln
 340 345 350
- Arg Glu Gly His Leu Lys Tyr Ser Thr Thr Val Gly Gln Tyr Arg Ser

355

360

365

Asn Ser Tyr Asn Gln Lys Ser Pro Tyr Val Phe Gln Gly Glu Leu Ile 370 375 380

Trp Gly Leu Pro Trp Asp Ile Thr Ala Tyr Gly Gly Ala Gln Phe Ser 390 395 400

Glu Asp Tyr Arg Ala Leu Ala Leu Gly Leu Gly Leu Asn Leu Gly Val
405
415

Phe Gly Ala Thr Ser Phe Asp Val Thr Gln Ala Asn Ser Ser Leu Val 420 425 430

Asp Gly Ser Lys His Gln Gly Gln Ser Tyr Arg Phe Leu Tyr Ser Lys

Ser Leu Val Gln Thr Gly Thr Ala Phe His Ile Ile Gly Tyr Arg Tyr 450 455 460

Ser Thr Gln Gly Phe Tyr Thr Leu Ser Asp Thr Thr Tyr Gln Gln Met 470 475 480

Ser Gly Thr Val Val Asp Pro Lys Thr Leu Asp Asp Lys Asp Tyr Val

Tyr Asn Trp Asn Asp Phe Tyr Asn Leu Arg Tyr Ser Lys Arg Gly Lys
500 505 510

Phe Gln Ala Ser Val Ser Gln Pro Phe Gly Asn Tyr Gly Ser Met Tyr 515 520 525

Leu Ser Ala Ser Gln Gln Thr Tyr Trp Asn Thr Asp Lys Lys Asp Ser
530 535 540

Leu Tyr Gln Val Gly Tyr Asn Thr Ser Ile Lys Gly Ile Tyr Leu Asn 545 550 555 560

Val Ala Trp Asn Tyr Ser Lys Ser Pro Gly Thr Asn Ala Asp Lys Ile
565 570

Val Ser Leu Asn Val Ser Leu Pro Ile Ser Asn Trp Leu Ser Ser Thr
580 585 590

- Asn Asp Gly Arg Ser Ser Ser Asn Ala Met Thr Ala Thr Tyr Gly Tyr 595 600 605
- Ser Gln Asp Asn His Gly Gln Val Asn Gln Tyr Thr Gly Val Ser Gly 610 615 620
- Ser Leu Leu Glu Gln His Asn Leu Ser Tyr Asn Ile Gln His Gly Phe 625 630 635 640
- Ala Asn Gln Asp Asn Ser Ser Ser Gly Ser Val Gly Val Asn Tyr Arg
 645 650 655
- Gly Ala Tyr Gly Ser Leu Asn Ser Ala Tyr Ser Tyr Asp Asn Glu Gly 660 665 670
- Asn Gln Gln Ile Asn Tyr Gly Ile Ser Gly Ala Leu Val Val His Glu 675 680 685
- Asn Gly Leu Thr Leu Ser Gln Pro Leu Gly Glu Thr Asn Val Leu Ile 690 695 700
- Lys Ala Pro Gly Ala Asn Asn Val Asp Val Gln Arg Gly Thr Gly Ile
 705 710 715 720
- Ser Thr Asp Trp Arg Gly Tyr Ala Val Val Pro Tyr Ala Thr Glu Tyr 725 730 735
- Arg Arg Asn Asn Ile Ser Leu Asp Pro Met Ser Met Asn Met His Thr 740 745 750
- Glu Leu Asp Ile Thr Ser Thr Glu Val Ile Pro Gly Lys Gly Ala Leu 755 760 , 765
- Val Arg Ala Glu Phe Ala Ala His Ile Gly Ile Arg Gly Leu Phe Thr 770 780
- Val Arg Tyr Arg Asn Lys Ser Val Pro Phe Gly Ala Thr Ala Ser Ala 785 790 795 800
- Gln Ile Lys Asn Ser Ser Gln Ile Thr Gly Ile Val Gly Asp Asn Gly 805 810 815

(F)

- Gln Leu Tyr Leu Ser Gly Leu Pro Leu Glu Gly Val Ile Asn Ile Gln 820
- Trp Gly Asp Gly Val Gln Gln Lys Cys Gln Ala Asn Tyr Lys Leu Pro 840
- Glu Thr Glu Leu Asp Asn Pro Val Ser Tyr Ala Thr Leu Glu Cys Arg

- <210> 19 <211> 169 <212> PRT <213> Escherichia coli <400> 19
- Met Gly Ala Ile Tyr Val Lys Arg Leu Ile Leu Ser Val Ala Leu Ile 5 . 10
- Ile Pro Ile Ala Ser Asn Ala Ser Asp Ala Leu Asn Gln Pro Ser Ser 25
- Ser Leu Asn Asp Gly Val Glu Thr Phe Phe Ile Ser Cys Phe Asp Met 40
- Pro Gln Glu Thr Thr Asp Met Asp Ala Cys Gln Arg Val Gln Leu 50
- Ala Gln Val Ser Trp Val Lys Asn Lys Tyr Ser Val Ala Ala Leu Asn 75
- Arg Leu Lys Gln Asp Asn Lys Asp Asp Pro Gln Arg Leu Gln Glu Leu 85
- Thr Ala Ser Phe Asn Ala Glu Ser Glu Ala Trp Thr Glu Leu Ile Glu 100
- Lys Ala Ser Lys Ser Val Gln Val Asp Tyr Val Gly Gly Thr Ile Ala 115 120
- Gly Thr Ala Val Ala Ser Arg Gln Ile Gly L'eu Leu Glu Leu Gln Ser 130 135
- His Asp Ile Trp Glu His Trp Leu Arg Ser Arg Gly Leu Asn Ser Ser 145 150 155

Ser Phe Ala Arg Thr Lys Val Gln Ile 165

<210> 20

<211> 713

<212> PRT

<213> Escherichia coli

<400> 20

Met Ala Met Phe Thr Pro Ser Phe Ser Gly Leu Lys Gly Arg Ala Leu 1 5 10 15

Phe Ser Leu Leu Phe Ala Ala Pro Met Ile His Ala Thr Asp Ser Val 20 25 30

Thr Thr Lys Asp Gly Glu Thr Ile Thr Val Thr Ala Asp Ala Asn Thr 35 40 45

Ala Thr Glu Ala Thr Asp Gly Tyr Gln Pro Leu Ser Thr Ser Thr Ala 50 55 60

Thr Leu Thr Asp Met Pro Met Leu Asp Ile Pro Gln Val Val Asn Thr 65 70 75 80

Val Ser Asp Gln Val Leu Glu Asn Gln Asn Ala Thr Thr Leu Asp Glu 85 90 95

Ala Leu Tyr Asn Val Ser Asn Val Val Gln Thr Asn Thr Leu Gly Gly
100 105 110

Thr Gln Asp Ala Phe Val Arg Gly Phe Gly Ala Asn Arg Asp Gly 115 120 125

Ser Ile Met Thr Asn Gly Leu Arg Thr Val Leu Pro Arg Ser Phe Asn 130 135 140

Ala Ala Thr Glu Arg Val Glu Val Leu Lys Gly Pro Ala Ser Thr Leu 145 150 155 160

Tyr Gly Ile Leu Asp Pro Gly Gly Leu Ile Asn Val Val Thr Lys Arg

Pro Glu Lys Thr Phe His Gly Ser Val Ser Ala Thr Ser Ser Ser Phe

180 185 190

Gly Gly Gly Thr Gly Gln Leu Asp Ile Thr Gly Pro Ile Glu Gly Thr
195 200 205

Gln Leu Ala Tyr Arg Leu Thr Gly Glu Val Gln Asp Glu Asp Tyr Trp 210 215 220

Arg Asn Phe Gly Lys Glu Arg Ser Thr Phe Ile Ala Pro Ser Leu Thr 225 230 235 240

Trp Phe Gly Asp Asn Ala Thr Val Thr Met Leu Tyr Ser His Arg Asp 245 250 255

Tyr Lys Thr Pro Phe Asp Arg Gly Thr Ile Phe Asp Leu Thr Thr Lys 260 265 270

Gln Pro Val Asn Val Asp Arg Lys Ile Arg Phe Asp Glu Pro Phe Asn 275 280 285

Ile Thr Asp Gly Gln Ser Asp Leu Ala Gln Leu Asn Ala Glu Tyr His 290 295 300

Leu Asn Ser Gln Trp Thr Ala Arg Phe Asp Tyr Ser Tyr Ser Gln Asp 305 310 315 320

Lys Tyr Ser Asp Asn Gln Ala Arg Val Thr Ala Tyr Asp Ala Thr Thr 325 330 335

Gly Thr Leu Thr Arg Arg Val Asp Ala Thr Gln Gly Ser Thr Gln Arg 340 345 350

Met His Ala Thr Arg Ala Asp Leu Gln Gly Asn Val Asp Ile Ala Gly 355

Phe Tyr Asn Glu Ile Leu Gly Gly Val Ser Tyr Glu Tyr Tyr Asp Leu 370 375 380

Leu Arg Thr Asp Met Ile Arg Cys Lys Lys Ala Lys Asp Phe Asn Ile 385 390 395 400

Tyr Asn Pro Val Tyr Gly Asn Thr Ser Lys Cys Thr Thr Val Ser Ala
405 410 415

שוופטספום. ...ייס

Ser Asp Ser Asp Gln Thr Ile Lys Gln Glu Asn Tyr Ser Ala Tyr Ala 420 425 430

Gln Asp Ala Leu Tyr Leu Thr Asp Asn Trp Ile Ala Val Ala Gly Ile 435 440 445

Arg Tyr Gln Tyr Tyr Thr Gln Tyr Ala Gly Lys Gly Arg Pro Phe Asn 450 450

Val Asn Thr Asp Ser Arg Asp Glu Gln Trp Thr Pro Lys Leu Gly Leu 465 470 475 480

Val Tyr Lys Leu Thr Pro Ser Val Ser Leu Phe Ala Asn Tyr Ser Gln 485 490 495

Thr Phe Met Pro Gln Ser Ser Ile Ala Ser Tyr Ile Gly Asp Leu Pro 500 505 510

Pro Glu Ser Ser Asn Ala Tyr Glu Val Gly Ala Lys Phe Glu Leu Phe 515 520 525

Asp Gly Ile Thr Ala Asp Ile Ala Leu Phe Asp Ile.His Lys Arg Asn 530 540

Val Leu Tyr Thr Glu Ser Ile Gly Asp Glu Thr Ile Ala Lys Thr Ala 545 550 555 560

Gly Arg Val Arg Ser Arg Gly Val Glu Val Asp Leu Ala Gly Ala Leu 565 570 575

Thr Glu Asn Ile Asn Ile Ile Ala Ser Tyr Gly Tyr Thr Asp Ala Lys 580 585 590

Val Leu Glu Asp Pro Asp Tyr Ala Gly Lys Pro Leu Pro Asn Val Pro 595 600 605

Arg His Thr Gly Ser Leu Phe Leu Thr Tyr Asp Ile His Asn Met Pro 610 620

Gly Asn Asn Thr Leu Thr Phe Gly Gly Gly His Gly Val Ser Arg 625 630 635 640

Arg Ser Ala Thr Asn Gly Ala Asp Tyr Tyr Leu Pro Gly Tyr Phe Val 645 650 655

Ala Asp Ala Phe Ala Ala Tyr Lys Met Lys Leu Gln Tyr Pro Val Thr 660 665 670

Leu Gln Leu Asn Val Lys Asn Leu Phe Asp Lys Thr Tyr Tyr Thr Ser 675 680 685

Ser Ile Ala Thr Asn Asn Leu Gly Asn Gln Ile Gly Asp Pro Arg Glu 690 695 700

Val Gln Phe Thr Val Lys Met Glu Phe 705 710

<210> 21

<211> 606

<212> PRT

<213> Escherichia coli

<400> 21

פאופחחמים: אווח

Met Lys Ile Ser Trp Asn Tyr Ile Phe Lys Asn Lys Trp Arg Phe Hist 1 5 10 15

Ile Thr Ser Ile Ser Leu Phe Leu Ile Met Leu Ala Val Ser Ile Ala 20 25 30

Phe Leu His Leu Arg Phe Asn Thr Leu Ser Ser Thr Asp Lys Met Arg 35 40 45

Leu Glu Met Tyr Lys Ser Thr Leu Tyr Ser Thr Ile Glu Gln Phe Tyr 50 55 60

Val Leu Pro Tyr Met Leu Ser Thr Asp His Ile Ile Arg Gln Ala Val 65 70 75 80

Ile Thr Pro Asp Asp Met Thr Ser Ser Glu Leu Asn Gln Arg Ile Ala 85 90 95

His Phe Asn Thr Gln Leu Lys Thr Ala Ala Ile Phe Ile Leu Asp Thr 100 105 110

Gln Gly Lys Ala Ile Ala Ser Ser Asn Trp Gln Asp Pro Gly Ser Tyr
115 120 125

Val	Gly 130	Gln	Āsn	Tyr	Ser	Tyr 135	Arg	Pro	Тут	Tyr	Lys 140	His	Ala	Met	Ser
Gly 145	Leu	Asn	Gly	Arg	Phe 150	Tyr	Gly	Ile	Gly	Ser 155	Thr	Thr	Asn	Thr	Pro 160
Gly	Phe	Phe	Leu	Ser 165	Thr	Ser	Ile	Lys	Asp 170	Lys	Gly	Lys	Ile	Val 175	Gly
Val	Val	Val	Val 180	Lys	Ile	Ser	Leu	Asn 185	Glu	Ile	Glu	Lys	Ala 190	Trp	Ala
Glu	Gly	Pro 195	Glu	Asn	Ile	Ile	Val 200	Asn	Asp	Glu	His	Gly 205	Ile	Ile	Phe
Leu	Ser 210	Ser	Lys	Ser	Pro	Trp 215	Arg	Met	Arg	Thr	Leu 220	Gln	Pro	Leu	Pro
Val 225	Gln	Ala	Lys	Gln	Lys 230	Leu	Gln	Ser	Thr	Arg 235	Gln	Tyr	Ser	Leu	Asp 240
Asn	Leu	Leu	Pro	Ala 245	Asp	Tyr	Tyr.	Pro	Cys 250	Tyr	Thr	Val	Ser	Asn 255	Phe
Thr	Phe	Leu	Lys 260	Asp	Lys	Lys	Glu	Gln 265	Leu	Cys	Leu	Phe	Pro 270	Gln	Tyr
Tyr	Thr	Gln 275	Gln	Ile	Ala	Ile	Pro 280	Glu	Phe	Asn	Trp	Lys 285	Met	Thr	Ile
Met	Val 290	Pro	Leu	Asp	Asn	Leu 295	Tyr	Trp	Ser	Trp	Ala 300	Ile	Ser	Leu	Val
Ile 305	Thr	Leu	Ile	Ile	Tyr 310	Leu	Leu	Phe	Leu	Leu 315	Phe	Ile	Lys	Tyr	Trp 320
Arg	Met	Arg	Ser	His 325	Ala	Gln	Gln	Leu	Leu 330	Thr	Leu	Ala	Asn	Glu 335	Thr
Leu	Glu	Lys	Gln	Val	Lys	Glu	Arg	Thr	Ser	Ala	Leu	Glu	Leu	Ile	Asn

340

- Gln Lys Leu Ile Gln Glu Ile Lys Glu Arg Ser Gln Ala Glu Gln Val 355 360 365
- Leu Gln Ile Thr Arg Ser Glu Leu Ala Glu Ser Ser Lys Leu Ala Ala 370 380
- Leu Gly Gln Met Ala Thr Glu Ile Ala His Glu Gln Asn Gln Pro Leu 385 390 395 400
- Ala Ala Ile His Ala Leu Thr Asp Asn Ala Arg Thr Met Leu Lys Lys
 405 410 415
- Glu Met Tyr Pro Gln Val Glu Gln Asn Leu Lys His Ile Ile Ser Val 420 425 430
- Ile Glu Arg Met Thr Gln Leu Ile Ser Glu Leu Lys Ala Phe Ala Ser 435 440 445
- Arg His Arg Val Pro Lys Gly Ser Ala Asp Val Ile Lys Val Met Tyr 450 455 460
- Ser Ala Val Ala Leu Leu Asn His Ser Met Glu Lys Asn Asn Ile Glu 465 470 475 480
- Arg Arg Ile Lys Ala Pro Ser Met Pro Leu Phe Val Asn Cys Asp Glu 485 490 495
- Leu Gly Leu Glu Gln Ile Phe Ser Asn Leu Ile Ser Asn Ala Leu Asp 500 505 510
- Ser Met Glu Gly Ser Ser Tyr Lys Arg Leu Asp Ile Ala Ile Arg Gln 515 520 525
- Ala Asn Asn Lys Val Ile Ile Thr Ile Lys Asp Ser Gly Gly Gly Phe 530 540
- Ala Pro Glu Val Val Asp Arg Ile Phe Glu Pro Phe Phe Thr Thr Lys 545 550 555 560
- Arg Arg Gly Met Gly Leu Gly Leu Ala Ile Val Ser Glu Ile Val Arg 565 570 575

Asn Ser Asn Gly Ala Leu His Ala Ser Asn His Pro Glu Gly Gly Ala 580 585

Val Met Thr Leu Thr Trp Pro Glu Trp Gly Glu Glu His Glu 600

<210> 22

<211> 101 <212> PRT <213> Escherichia coli <400> 22

Val Leu Thr Pro Gln His Leu Arg Cys Val Leu Thr Cys Ser Asp Leu

Leu Thr Leu Leu Ser Gly Thr Val Met Ser Gln Met Pro Leu Tyr Phe 25

Leu Asn Thr Gln Lys Lys Leu Thr Ala His Tyr Glu Trp Leu Gln Ile

Asn Leu Thr Asp Thr Tyr Glu Leu Val Lys Arg Leu Met Pro Ile Pro

Ser Leu Asp Val Val Lys Val Gly Lys Leu Val Leu Pro Glu Lys

Gly His His Gly Phe Tyr Pro Glu Ala Gly Val Val Tyr Arg Thr Val

Ala Pro Glu Asn Pro 100

<210> 23

<211> 263

<212> PRT <213> Escherichia coli <400> 23

Met Met Lys Asn Thr Gly Tyr Ile Leu Ala Leu Cys Leu Thr Ala Ser

Gly His Val Leu Ala His Asp Val Trp Ile Thr Gly Lys Gln Ala Glu 25

Asn Asn Val Thr Ala Glu Ile Gly Tyr Gly His Asn Phe Pro Ser Lys

40

45

Gly Thr Ile Pro Asp Arg Arg Asp Phe Phe Glu Asn Pro Arg Leu Tyr 50 55 60

Asn Gly Lys Glu Thr Ile Thr Leu Lys Pro Ala Ser Thr Asp Tyr Val

Tyr Lys Thr Glu Ser Ala Ser Lys Asp Asn Gly Tyr Val Leu Ser Thr

Tyr Met Lys Pro Gly Tyr Trp Ser Arg Thr Ser Ser Gly Trp Lys Pro

Val Ser Arg Glu Gly Arg Asn Asp Val Ala Tyr Cys Glu Phe Val Thr 115 120 125

Lys Tyr Ala Lys Ser Phe Ile Pro Gly Glu Gln Gln Met Pro Ala Gln 130 135 140

Leu Tyr Gln Ser Pro Thr Gly His Glu Leu Glu Ile Ile Pro Leu Ser 150 155 160

Asp Ile Ser Arg Phe Ser Glu Asn Val Lys Leu Lys Val Leu Tyr Lys
165 170 175

Thr Ser Pro Leu Ala Gly Ala Ile Met Glu Leu Asp Ser Val Ser Tyr
180 185 190

Leu Thr Ser Ser Arg His Thr His Ala Val Glu His Lys His Pro Val

His Lys Ala Glu Leu Thr Phe Val Thr Asn Glu Asp Gly Ile Val Thr

Val Pro Ser Leu His Ile Gly Gln Trp Leu Ala Lys Val Gln Asn Lys
225 230 235 240

Lys Ser Phe Gln Asp Lys Ser Leu Cys Asp Glu Thr Val Asp Val Ala 245 250 255

Thr Leu Ser Phe Ser Arg Asn 260

- <210> 24 <211> 378 <212> PRT <213> Escherichia coli <400> 24
- Met Gly Lys Ile Lys Tyr Trp Leu Ile Val Gly Phe Ile Ile Leu Phe
- Ala Ile Phe Tyr Ile Ala Ile Ser Asp Arg Asp Ser Thr Leu Ser Arg
- Leu Lys Ser Ala Gly Glu Asn Gly Asp Val Glu Ala Gln Tyr Ala Leu
- Gly Leu Met Tyr Leu Tyr Gly Glu Ile Leu Asp Val Asp Tyr Gln Gln
- Ala Lys Ile Trp Tyr Glu Lys Ala Ala Asp Gln Asn Asp Pro Arg Ala
- Gln Ala Lys Leu Gly Val Met Tyr Ala Asn Gly Leu Gly Val Asn Gln
- Asp Tyr Gln Gln Ser Lys Leu Trp Tyr Glu Lys Ala Ala Ala Gln Asn 105
- Asp Val Asp Ala Gln Phe Leu Leu Gly Glu Met Tyr Asp Asp Gly Leu
- Gly Val Ser Gln Asp Tyr Gln His Ala Lys Met Trp Tyr Glu Lys Ala
- Ala Ala Gln Asn Asp Glu Arg Ala Gln Val Asn Leu Ala Val Leu Tyr 145 150
- Ala Lys Gly Asn Gly Val Glu Gln Asp Tyr Arg Gln Ala Lys Ser Trp 165 170
- Tyr Glu Lys Ala Ala Ala Gln Asn Ser Pro Asp Ala Gln Phe Ala Leu 185
- Gly Ile Leu Tyr Ala Asn Ala Asn Gly Val Glu Gln Asp Tyr Gln Gln

200

205

Ala Lys Asp Trp Tyr Glu Lys Ala Ala Glu Gln Asn Phe Ala Asn Ala 215

Gln Phe Asn Leu Gly Met Leu Tyr Tyr Lys Gly Glu Gly Val Lys Gln 235

Asn Phe Arg Gln Ala Arg Glu Trp Phe Glu Lys Ala Ala Ser Gln Asn

Gln Pro Asn Ala Gln Tyr Asn Leu Gly Gln Ile Tyr Tyr Gly Gln 260 265

Gly Val Thr Gln Ser Tyr Arg Gln Ala Lys Asp Trp Phe Glu Lys Ala 280

Ala Glu Lys Gly His Val Asp Ala Gln Tyr Asn Leu Gly Val Ile Tyr 290 295

Glu Asn Gly Glu Gly Val Ser Gln Asn Tyr Gln Gln Ala Lys Ala Trp 315

Tyr Glu Lys Ala Ala Ser Gln Asn Asp Ala Gln Ala Gln Phe Glu Leu 325

Gly Val Met Asn Glu Leu Gly Gln Gly Glu Ser Ile Asp Leu Lys Gln 340

Ala Arg His Tyr Tyr Glu Arg Ser Cys Asn Asn Gly Leu Lys Lys Gly

Cys Glu Arg Leu Lys Glu Leu Tyr Lys 370 375

<210> 25

<211> 654

<212> PRT

<213> Escherichia coli <400> 25

27.622610 1110

Met Asn Val Ile Arg Thr Val Ile Cys Thr Leu Ile Ile Leu Pro Val 5

1.13

- Gly Leu Gln Ala Ala Thr Ser His Ser Ser Met Val Lys Asp Thr Ile 20 25 30
- Thr Ile Val Ala Thr Gly Asn Gln Asn Thr Val Phe Glu Thr Pro Ser 35 40 45
- Met Val Ser Val Val Thr Asn Asp Thr Pro Trp Ser Gln Asn Ala Val 50 55 60
- Thr Ser Ala Gly Met Leu Lys Gly Val Ala Gly Leu Ser Gln Thr Gly 65 70 75 80
- Ala Gly Arg Thr Asn Gly Gln Thr Phe Asn Leu Arg Gly Tyr Asp Lys 85 90 95
- Ser Gly Val Leu Val Leu Val Asp Gly Val Arg Gln Leu Ser Asp Met 100 105 110
- Ala Lys Ser Ser Gly Thr Tyr Leu Asp Pro Ala Leu Val Lys Arg Ile 115 120 125
- Glu Val Val Arg Gly Pro Asn Ser Ser Leu Tyr Gly Ser Gly Gly Leu 130 135 140
- Gly Gly Val Val Asp Phe Arg Thr Ala Asp Ala Ala Asp Phe Leu Pro 145 150 155 160
- Pro Gly Glu Thr Asn Gly Leu Ser Leu Trp Gly Asn Ile Ala Ser Gly 165 170 175
- Asp His Ser Thr Gly Ser Gly Leu Thr Trp Phe Gly Lys Thr Gly Lys 180 185 190
- Thr Asp Ala Leu Leu Ser Val Ile Met Arg Lys Arg Gly Asn Ile Tyr 195 200 205
- Gln Ser Asp Gly Glu His Ala Pro Asn Lys Glu Lys Pro Ala Ala Leu 210 215 220
- Phe Ala Lys Gly Ser Val Gly Ile Thr Asp Ser Asn Lys Ala Gly Ala 225 230 235 240
- Ser Leu Arg Leu Tyr Arg Asn Asn Thr Thr Glu Pro Gly Asn Ser Thr

.

245

250

255

Gln Thr His Gly Asp Ser Gly Leu Arg Asp Arg Lys Thr Val Gln Asn 260 265 270

Asp Val Gln Phe Trp Tyr Gln Tyr Ala Pro Val Asp Asn Ser Leu Ile 275 280 285

Asn Val Lys Ser Thr Leu Tyr Leu Ser Asp Ile Thr Ile Lys Thr Asn 290 295 300

Gly His Asn Lys Thr Ala Glu Trp Arg Asn Asn Arg Thr Ser Gly Val

Asn Val Val Asn Arg Ser His Thr Leu Ile Phe Pro Gly Ala His Gln 325 330 335

Leu Ser Tyr Gly Ala Glu Tyr Tyr Arg Gln Gln Gln Lys Pro Glu Gly 340 345 350

Ser Ala Thr Leu Tyr Pro Glu Gly Asn Ile Asp Phe Thr Ser Leu Tyr 355 360 365

Phe Gln Asp Glu Met Thr Met Lys Ser Tyr Pro Val Asn Ile Ile Val 370 375 380

Gly Ser Arg Tyr Asp Arg Tyr Lys Ser Phe Asn Pro Arg Ala Gly Glu
385 390 395

Leu Lys Ala Glu Arg Leu Ser Pro Arg Ala Ala Ile Ser Val Ser Pro
405 410 415

Thr Asp Trp Leu Met Met Tyr Gly Ser Ile Ser Ser Ala Phe Arg Ala 420 425 430

Pro Thr Met Ala Glu Met Tyr Arg Asp Asp Val His Phe Tyr Arg Lys
435 440 445

Gly Lys Pro Asn Tyr Trp Val Pro Asn Leu Asn Leu Lys Pro Glu Asn 450

Asn Ile Thr Arg Glu Ile Gly Ala Gly Ile Gln Leu Asp Gly Leu Leu 465 470 475

Thr Asp Asn Asp Arg Leu Gln Leu Lys Gly Gly Tyr Phe Gly Thr Asp 485 490 495

Ala Arg Asn Tyr Ile Ala Thr Arg Val Asp Met Lys Arg Met Arg Ser 500 505 510

Tyr Ser Tyr Asn Val Ser Arg Ala Arg Ile Trp Gly Trp Asp Met Gln 515 520 525

Gly Asn Tyr Gln Ser Asp Tyr Val Asp Trp Met Leu Ser Tyr Asn Arg 530 540

Thr Glu Ser Met Asp Ala Ser Ser Arg Glu Trp Leu Gly Ser Gly Asn 545 550 555 560

Pro Asp Thr Leu Ile Ser Asp Ile Ser Ile Pro Val Gly His Arg Gly 565 570 575

Val Tyr Ala Gly Trp Arg Ala Glu Leu Ser Ala Ser Ala Thr His Val 580 585 590

Lys Lys Gly Asp Pro His Gln Ala Gly Tyr Thr Ile His Ser Phe Ser 595 600 605

Leu Ser Tyr Lys Pro Val Ser Val Lys Gly Phe Glu Ala Ser Val Thr 610 615 620

Leu Asp Asn Ala Phe Asn Lys Leu Ala Met Asn Gly Lys Gly Val Pro 625 630 635 640

Leu Ser Gly Arg Thr Val Ser Leu Tyr Thr Arg Tyr Gln Trp 645 : 650

<210> 26

<211> 1376

<212> PRT

<213> Escherichia coli

<400> 26

BHCDOCIO- MIC

Met Asn Lys Ile Tyr Ala Leu Lys Tyr Cys Tyr Ile Thr Asn Thr Val 1 5 10 15

Lys Val Val Ser Glu Leu Ala Arg Arg Val Cys Lys Gly Ser Thr Arg

30

Arg Gly Lys Arg Leu Ser Val Leu Thr Ser Leu Ala Leu Ser Ala Leu 35 40 45

25

Leu Pro Thr Val Ala Gly Ala Ser Thr Val Gly Gly Asn Asn Pro Tyr 50 55 60

Gln Thr Tyr Arg Asp Phe Ala Glu Asn Lys Gly Gln Phe Gln Ala Gly 65 70 75 80

Ala Thr Asn Ile Pro Ile Phe Asn Asn Lys Gly Glu Leu Val Gly His 85 90 95

Leu Asp Lys Ala Pro Met Val Asp Phe Ser Ser Val Asn Val Ser Ser 100 110

Asn Pro Gly Val Ala Thr Leu Ile Asn Pro Gln Tyr Ile Ala Ser Val

Lys His Asn Lys Gly Tyr Gln Ser Val Ser Phe Gly Asp Gly Gln Asn 130 135 140

Ser Tyr His Ile Val Asp Arg Asn Glu His Ser Ser Ser Asp Leu His 145 150 155 160

Thr Pro Arg Leu Asp Lys Leu Val Thr Glu Val Ala Pro Ala Thr Val 165 170 175

Thr Ser Ser Ser Thr Ala Asp Ile Leu Asn Pro Ser Lys Tyr Ser Ala 180 185 190

Phe Tyr Arg Ala Gly Ser Gly Ser Gln Tyr Ile Gln Asp Ser Gln Gly 195 200 205

Lys Arg His Trp Val Thr Gly Gly Tyr Gly Tyr Leu Thr Gly Gly Ile 210 215 220

Leu Pro Thr Ser Phe Phe Tyr His Gly Ser Asp Gly Ile Gln Leu Tyr 225 230 235 235

Met Gly Gly Asn Ile His Asp His Ser Ile Leu Pro Ser Phe Gly Glu 245 250 255

- Ala Gly Asp Ser Gly Ser Pro Leu Phe Gly Trp Asn Thr Ala Lys Gly 260 265 270
- Gln Trp Glu Leu Val Gly Val Tyr Ser Gly Val Gly Gly Gly Thr Asn 275 280 285
- Leu Ile Tyr Ser Leu Ile Pro Gln Ser Phe Leu Ser Gln Ile Tyr Ser 290 295 300
- Glu Asp Asn Asp Ala Pro Val Phe Phe Asn Ala Ser Ser Gly Ala Pro 305 310 315 320
- Leu Gln Trp Lys Phe Asp Ser Ser Thr Gly Thr Gly Ser Leu Lys Gln 325 330 335
- Gly Ser Asp Glu Tyr Ala Met His Gly Gln Lys Gly Ser Asp Leu Asn 340 345 350
- Ala Gly Lys Asn Leu Thr Phe Leu Gly His Asn Gly Gln Ile Asp Leu 355 360 365
- Glu Asn Ser Val Thr Gln Gly Ala Gly Ser Leu Thr Phe Thr Asp Asp 370 375 380
- Tyr Thr Val Thr Thr Ser Asn Gly Ser Thr Trp Thr Gly Ala Gly Ile 385 390 395 400
- Ile Val Asp Lys Asp Ala Ser Val Asn Trp Gln Val Asn Gly Val Lys
 405 410 415
- Gly Asp Asn Leu His Lys Ile Gly Glu Gly Thr Leu Val Val Gln Gly 420 425 430
- Thr Gly Val Asn Glu Gly Gly Leu Lys Val Gly Asp Gly Thr Val Val 435
- Leu Asn Gln Gln Ala Asp Ser Ser Gly His Val Gln Ala Phe Ser Ser 450 455 460
- Val Asn Ile Ala Ser Gly Arg Pro Thr Val Val Leu Ala Asp Asn Gln 465 470 475 480

- Gln Val Asn Pro Asp Asn Ile Ser Trp Gly Tyr Arg Gly Gly Val Leu 485 490 495
- Asp Val Asn Gly Asn Asp Leu Thr Phe His Lys Leu Asn Ala Ala Asp 500 505 510
- Tyr Gly Ala Thr Leu Gly Asn Ser Ser Asp Lys Thr Ala Asn Ile Thr 515 520 525
- Leu Asp Tyr Gln Thr Arg Pro Ala Asp Val Lys Val Asn Glu Trp Ser 530 535 540
- Ser Ser Asn Arg Gly Thr Val Gly Ser Leu Tyr Ile Tyr Asn Asn Pro 545 550 555 560
- Tyr Thr His Thr Val Asp Tyr Phe Ile Leu Lys Thr Ser Ser Tyr Gly 565 570 575
- Trp Phe Pro Thr Gly Gln Val Ser Asn Glu His Trp Glu Tyr Val Gly 580 585 590
- His Asp Gln Asn Ser Ala Gln Ala Leu Leu Ala Asn Arg Ile Asn Asn 595 600 605
- Lys Gly Tyr Leu Tyr His Gly Lys Leu Leu Gly Asn Ile Asn Phe Ser 610 620
- Asn Lys Ala Thr Pro Gly Thr Thr Gly Ala Leu Val Met Asp Gly Ser 625 635 640
- Ala Asn Met Ser Gly Thr Phe Thr Gln Glu Asn Gly Arg Leu Thr Ile 645 650 655
- Gln Gly His Pro Val Ile His Ala Ser Thr Ser Gln Ser Ile Ala Asn 660 665 670
- Thr Val Ser Ser Leu Gly Asp Asn Ser Val Leu Thr Gln Pro Thr Ser 675 680 685
- Phe Thr Gln Asp Asp Trp Glu Asn Arg Thr Phe Ser Phe Gly Ser Leu 690 695 700

Val	Leu	Lys	Asp	Thr	Asp	Phe	Gly	Leu	Gly	Arg	Asn	Ala	Thr	Leu	Asn
705					710				_	715					720

- Thr Thr Ile Gln Ala Asp Asn Ser Ser Val Thr Leu Gly Asp Ser Arg
 725 730 735
- Val Phe Ile Asp Lys Lys Asp Gly Gln Gly Thr Ala Phe Thr Leu Glu
 740 745 750
- Glu Gly Thr Ser Val Ala Thr Lys Asp Ala Asp Lys Ser Val Phe Asn 755 760 765
- Gly Thr Val Asn Leu Asp Asn Gln Ser Val Leu Asn Ile Asn Glu Ile 770 780
- Phe Asn Gly Gly Ile Gln Ala Asn Asn Ser Thr Val Asn Ile Ser Ser 785 790 795 800
- Asp Ser Ala Val Leu Glu Asn Ser Thr Leu Thr Ser Thr Ala Leu Asn 805 : 810 815
- Leu Asn Lys Gly Ala Asn Val Leu Ala Ser Gln Ser Phe Val Ser Asp 820 825 830
- Gly Pro Val Asn Ile Ser Asp Ala Thr Leu Ser Leu Asn Ser Arg Pro 835 840 845
- Asp Glu Val Ser His Thr Leu Leu Pro Val Tyr Asp Tyr Ala Gly Ser 850 850
- Trp Asn Leu Lys Gly Asp Asp Ala Arg Leu Asn Val Gly Pro Tyr Ser 865 870 875 880
- Met Leu Ser Gly Asn Ile Asn Val Gln Asp Lys Gly Thr Val Thr Leu 885 890 895
- Gly Glu Glu Glu Leu Ser Pro Asp Leu Thr Leu Gln Asn Gln Met 900 905 910
- Leu Tyr Ser Leu Phe Asn Gly Tyr Arg Asn Thr Trp Ser Gly Ser Leu 915 920 925
- Asn Ala Pro Asp Ala Thr Val Ser Met Thr Asp Thr Gln Trp Ser Met

 $\left(\cdot \right)$

930

935

940

- Asn Gly Asn Ser Thr Ala Gly Asn Met Lys Leu Asn Arg Thr Ile Val 945 950 955 960
- Gly Phe Asn Gly Gly Thr Ser Ser Phe Thr Thr Leu Thr Thr Asp Asn 965 970 975
- Leu Asp Ala Val Gln Ser Ala Phe Val Met Arg Thr Asp Leu Asn Lys 980 985 990
- Ala Asp Lys Leu Val Ile Asn Lys Ser Ala Thr Gly His Asp Asn Ser 995 1000 1005
- Ilė Trp Val Asn Phe Leu Lys Lys Pro Ser Asp Lys Asp Thr Leu 1010 1015 1020
- Asp Ile Pro Leu Val Ser Ala Pro Glu Ala Thr Ala Asp Asn Leu 1025 1030 1035
- Phe Arg Ala Ser Thr Arg Val Val Gly Phe Ser Asp Val Thr Pro 1040 1045 1050
- Thr Leu Ser Val Arg Lys Glu Asp Gly Lys Lys Glu Trp Val Leu 1055
- Asp Gly Tyr Gln Val Ala Arg Asn Asp Gly Gln Gly Lys Ala Ala 1070 1075 1080
- Ala Thr Phe Met His Ile Ser Tyr Asn Asn Phe Ile Thr Glu Val 1085
- Asn Asn Leu Asn Lys Arg Met Gly Asp Leu Arg Asp Ile Asn Gly
- Glu Ala Gly Thr Trp Val Arg Leu Leu Asn Gly Ser Gly Ser Ala 1115 1120 1125
- Asp Gly Gly Phe Thr Asp His Tyr Thr Leu Leu Gln Met Gly Ala 1130 1140
- Asp Arg Lys His Glu Leu Gly Ser Met Asp Leu Phe Thr Gly Val

MEDOCID: AMO

Contract the first of the contract of the cont

Met Ala Thr Tyr Thr Asp Thr Asp Ala Ser Ala Gly Leu Tyr Ser 1160 1165 1170 Gly Lys Thr Lys Ser Trp Gly Gly Gly Phe Tyr Ala Ser Gly Leu 1180 1185 Phe Arg Ser Gly Ala Tyr Phe Asp Leu Ile Ala Lys Tyr Ile His 1190 1195 1200 Asn Glu Asn Lys Tyr Asp Leu Asn Phe Ala Gly Ala Gly Lys Gln 1210 Asn Phe Arg Ser His Ser Leu Tyr Ala Gly Ala Glu Val Gly Tyr 1225 Arg Tyr His Leu Thr Asp Thr Thr Phe Val Glu Pro Gln Ala Glu 1240 Leu Val Trp Gly Arg Leu Gln Gly Gln Thr Phe Asn Trp Asn Asp 1250 1255 1260 Ser Gly Met Asp Val Ser Met Arg Arg Asn Ser Val Asn Pro Leu 1265 1270 1275 Val Gly Arg Thr Gly Val Val Ser Gly Lys Thr Phe Ser Gly Lys 1285 Asp Trp Ser Leu Thr Ala Arg Ala Gly Leu His Tyr Glu Phe Asp 1300 Leu Thr Asp Ser Ala Asp Val His Leu Lys Asp Ala Ala Gly Glu 1315 His Gln Ile Asn Gly Arg Lys Asp Gly Arg Met Leu Tyr Gly Val 1325 1335 Gly Leu Asn Ala Arg Phe Gly Asp Asn Thr Arg Leu Gly Leu Glu Val Glu Arg Ser Ala Phe Gly Lys Tyr Asn Thr Asp Asp Ala Ile

 $(\mathcal{M}(X) \cap \mathcal{M}(Y)) = (\mathcal{M}(X) \cap \mathcal{M}(Y))$

Asn Ala Asn Ile Arg Tyr Ser Phe 1370 1375

<210> 27

<211> 349

<212> PRT

<213> Escherichia coli

<400> 27

Met Ile Thr Leu Phe Arg Leu Leu Ala Ile Leu Cys Leu Phe Phe Asn 1 5 10 10 15

Val Ser Ala Phe Ala Val Asp Cys Tyr Gln Asp Gly Tyr Arg Gly Thr 20 25 30

Thr Leu Ile Asn Gly Asp Leu Pro Thr Phe Lys Ile Pro Glu Asn Ala

Gln Pro Gly Gln Lys Ile Trp Glu Ser Gly Asp Ile Asn Ile Thr Val 50 55 60

Tyr Cys Asp Asn Ala Pro Gly Trp Ser Ser Asn Asn Pro Ser Glu Asn 65 70 75 80

Val Tyr Ala Trp Ile Lys Leu Pro Gln Ile Asn Ser Ala Asp Met Leu 85 90 95

Asn Asn Pro Tyr Leu Thr Phe Gly Val Thr Tyr Asn Gly Val Asp Tyr 100 105 110

Glu Gly Thr Asn Glu Lys Ile Asp Thr His Ala Cys Leu Asp Lys Tyr
115 120 125

Glu Gln Tyr Tyr Asn Gly Tyr Tyr His Asp Pro Val Cys Asn Gly Ser 130 135 140

Thr Leu Gln Lys Asn Val Thr Phe Asn Ala His Phe Arg Val Tyr Val 145 150 155 160

Lys Phe Lys Ser Arg Pro Ala Gly Asp Gln Thr Val Asn Phe Gly Thr

Val Asn Val Leu Gln Phe Asp Gly Glu Gly Gly Ala Asn Met Ala Pro 180 185 190 Asn Ala Lys Asn Leu Arg Tyr Ala Ile Thr Gly Leu Asp Asn Ile Ser 195 200 205

Phe Leu Asp Cys Ser Val Asp Val Arg Ile Ser Pro Glu Ser Gln Ile 210 215 220

Val Asn Phe Gly Gln Ile Ala Ala Asn Ser Ile Ala Thr Phe Pro Pro 225 230 235 240

Lys Ala Ala Phe Ser Val Ser Thr Ile Lys Asp Ile Ala Ser Asp Cys 245 250 255

Thr Glu Gln Phe Asp Val Ala Thr Ser Phe Phe Thr Ser Asp Thr Leu 260 265 270

Tyr Asp Asn Thr His Leu Glu Ile Gly Asn Gly Leu Leu Met Arg Ile
275 280 285

Thr Asp Gln Lys Thr Gln Glu Asp Ile Lys Phe Asn Gln Phe Lys Leu 290 295 300

Phe Ser Thr Tyr Ile Pro Gly Gln Ser Ala Ala Met Ala Thr Arg Asp 305 310 315 320

Tyr Gln Ala Glu Leu Thr Gln Lys Pro Gly Glu Pro Leu Val Tyr Gly 325 330 335

Pro Phe Gln Lys Asp Leu Ile Val Lys Ile Asn Tyr His 340 345

<210> 28

<211> 840

<212> PRT

<213> Escherichia coli

<400> 28

Met Asn Asn Lys Asn Thr Phe Ser Arg Asp Lys Leu Ser His Ala Ile 1 5 10 15

Lys Asn Ala Leu Ser Gly Val Val Cys Ser Leu Leu Phe Val Leu Pro

Val His Ala Val Glu Phe Asn Val Asp Met Ile Asp Ala Glu Asp Arg

40

45

Glu Asn Ile Asp Ile Ser Arg Phe Glu Lys Lys Gly Tyr Ile Pro Pro 50 55 60

Gly Arg Tyr Leu Val Arg Val Gln Ile Asn Lys Asn Met Leu Pro Gln 65 70 75 80

Thr Leu Ile Leu Glu Trp Val Lys Ala Asp Asn Glu Ser Gly Ser Leu 85 90 95

Leu Cys Leu Thr Lys Glu Asn Leu Thr Asn Phe Gly Leu Asn Thr Glu
100 105 110

Phe Ile Glu Ser Leu Gln Asn Ile Ala Gly Ser Glu Cys Leu Asp Leu 115 120 125

Ser Gln Arg Gln Glu Leu Thr Thr Arg Leu Asp Lys Ala Thr Met Ile 130 135 140

Leu Ser Leu Ser Val Pro Gln Ala Trp Leu Lys Tyr Gln Ala Thr Asn 145 150 150

Trp Thr Pro Pro Glu Phe Trp Asp Thr Gly Ile Thr Gly Phe Ile Leu 165 170 175

Asp Tyr Asn Val Tyr Ala Ser Gln Tyr Ala Pro His His Gly Asp Ser 180 185 190

Thr Gln Asn Val Ser Ser Tyr Gly Thr Leu Gly Phe Asn Leu Gly Ala 195 200 205

Trp Arg Leu Arg Ser Asp Tyr Gln Tyr Asn Gln Asn Phe Ala Asp Gly 210 215 220

Arg Ser Val Asn Arg Asp Ser Glu Phe Ala Arg Thr Tyr Leu Phe Arg 225 230 235 240

Pro Ile Pro Ser Trp Ser Ser Lys Phe Thr Met Gly Gln Tyr Asp Leu 245 250 255

Ser Ser Asn Leu Tyr Asp Thr Phe His Phe Thr Gly Ala Ser Leu Glu 260 265 270

Ser	Asp _.	Glu 275	Ser	Met	Leu	Pro	Pro 280	Asp	Leu	Gln	Gly	Tyr 285	Ala	Pro	Gln
Ile	Thr 290	Gly	Ile	Ala	Gln	Th <i>r</i> 295	Asn	Ala	Lys	Val	Thr 300	Val	Ala	Gln	Asn
Gly 305	Arg	Val	Leu	Tyr	Gln 310	Thr	Thr	Val	Ala	Pro 315	Gly	Pro	Phe	Thr	Ile 320
Ser	Asp	Leu	Gly	Gln 325	Ser	Phe	Gln	Gly	Gln 330	Leu	Asp	Val	Thr	Val 335	Glu
Glu	Glu	Asp	Gly 340	Arg	Thr	Ser	Thr	Phe 345	Gln	Val	Gly	Ser	Ala 350	Ser	Ile
Pro	Tyr	Leu 355	Thr	Arg	Lys	Gly	Gln 360	Val	Arg	Tyr	Lys	Thr 365	Ser	Leu	Gly
Lys	Pro 370	Thr	Ser	Val	Gly	His 375	Asn	Asp	Ile	Asn	Asn 380	Pro	Phe	Phe	Trp
Thr 385	Ala	Glu	Ala	Ser	Trp 390	Gly	Trp	Leu	Asn	Asn 395	Val	Ser	Leu	Tyr	Gly 400
Gly	Gly	Met	Phe	Thr 405	Ala	Asp	Asp	Tyr	Gln 410	Ala	Ile	Thr	Thr	Gly 415	Ile
Gly	Phe	Asn	Leu 420	Asn	Gln	Phe	Gly	Ser 425	Leu	Ser	Phe	Asp	Val 430	Thr	Gly
Ala	Asp	Ala 435	Ser	Leu	Gln	Gln	Gln 440		Ser	Gly	Asn	Leu 445	Arg	Gly	Tyr
Ser	Tyr 450	Arg	Phe	Asn	Tyr	Ala 455	Lys	His	Phe	Glu	Ser 460	Thr	Gly	Ser	Gln
Ile 465	Thr	Phe	Ala	Gly	Tyr 470	Arg	Phe	Ser	Asp	Lys 475	Asp	Tyr	Val	Ser	Met 480
Ser	Glu	Tyr	Leu	Ser 485	Ser	Arg	Asn	Gly	Asp 490	Glu	Ser	Ile	Asp	Asn 495	Glu

- Lys Glu Ser Tyr Val Ile Ser Leu Asn Gln Tyr Phe Glu Thr Leu Glu 500 505 510
- Leu Asn Ser Tyr Leu Asn Val Thr Arg Asn Thr Tyr Trp Asp Ser Ala
 515 520 525
- Ser Asn Thr Asn Tyr Ser Val Ser Val Ser Lys Asn Phe Asp Ile Gly 530 540
- Asp Phe Lys Gly Ile Ser Ala Ser Leu Ala Val Ser Arg Ile Arg Trp 545 550 555 560
- Asp Asp Asp Glu Glu Asn Gln Tyr Tyr Phe Ser Phe Ser Leu Pro Leu
 565 570 575
- Gln Gln Asn Arg Asn Ile Ser Tyr Ser Met Gln Arg Thr Gly Ser Ser 580 585 590
- Asn Thr Ser Gln Met Ile Ser Trp Tyr Asp Ser Ser Asp Arg Asn Asn 595 600 605
- Ile Trp Asn Ile Ser Ala Ser Ala Thr Asp Asp Asn Ile Arg Asp Gly 610 620
- Glu Pro Thr Leu Arg Gly Ser Tyr Gln His Tyr Ser Pro Trp Gly Arg 625 630 635 640
- Leu Asn Ile Asn Gly Ser Val Gln Pro Asn Gln Tyr Asn Ser Val Thr 645 650 655
- Ala Gly Trp Tyr Gly Ser Leu Thr Ala Thr Arg His Gly Val Ala Leu 660 665 670
- His Asp Tyr Ser Tyr Gly Asp Asn Ala Arg Met Met Val Asp Thr Asp 675 680 685
- Gly Ile Ser Gly Ile Glu Ile Asn Ser Asn Arg Thr Val Thr Asn Gly 690 695 700
- Leu Gly Ile Ala Val Ile Pro Ser Leu Ser Asn Tyr Thr Thr Ser Met 705 710 715 720

PRISDOCIDE AND

Leu Arg Val Asn Asn Asn Asp Leu Pro Glu Gly Val Asp Val Glu Asn 725 730 735

Ser Val Ile Arg Thr Thr Leu Thr Gln Gly Ala Ile Gly Tyr Ala Lys

Leu Asn Ala Thr Thr Gly Tyr Gln Ile Val Gly Val Ile Arg Gln Glu
755 760 765

Asn Gly Arg Phe Pro Pro Leu Gly Val Asn Val Thr Asp Lys Ala Thr 770 780

Gly Lys Asp Val Gly Leu Val Ala Glu Asp Gly Phe Val Tyr Leu Ser
785 790 795 800

Gly Ile Gln Glu Asn Ser Ile Leu His Leu Thr Trp Gly Asp Asn Thr 805 810 815

Cys Glu Val Thr Pro Pro Asn Gln Ser Asn Ile Ser Glu Ser Ala Ile 820 825 830

Ile Leu Pro Cys Lys Thr Val Lys 835

<210> 29

<211> 169

<212> PRT

<213> Escherichia coli

<400> 29

Leu Met Asn Thr Lys Gln Ser Val Ala Gln Leu Ala Val Pro His Arg

1 10 15

Lys Arg Leu Ser Ser Thr Met Val Val Ala Leu Leu Cys Val Val 20 25 30

Ala Gly Ala Val Met Ile Asn Ala Ala Asp Phe Pro Ala Thr Ala Ile
35 40 45

Glu Thr Asp Pro Gly Ala Ser Ala Phe Pro Thr Phe Tyr Ala Cys Ala 50 55 60

Leu Ile Val Leu Ala Val Leu Leu Val Ile Arg Asp Leu Leu Gln Ala 70 75 80

Lys Pro Ala Ser Cys Ala Asn Ala Gln Glu Lys Pro Ala Phe Arg Lys . 85 90

Thr Ala Thr Gly Ile Ala Ala Thr Ala Phe Tyr Ile Val Ala Met Ser 105 . 110

Tyr Cys Gly Tyr Leu Ile Thr Thr Pro Val Phe Leu Ile Val Ile Met 120

Thr Leu Met Gly Tyr Arg Arg Trp Val Leu Thr Pro Gly Ile Ala Leu 135

Leu Leu Thr Ala Ile Leu Trp Leu Leu Phe Val Glu Ala Leu Gln Val

Pro Leu Pro Val Gly Thr Phe Phe Glu 165

<210> 30

<211> 311 <212> PRT

<213> Escherichia coli

<400> 30

BNISDOCID: JAIO

Met Val Leu Leu Ala Gly Ala Ala Leu Ser Ile Ala Pro Val Gln Ala 5

Ala Ser Tyr Pro Thr Lys Gln Ile Glu Leu Val Val Pro Tyr Ala Ala 25 30

Gly Gly Gly Thr Asp Leu Val Ala Arg Ala Phe Ala Asp Ala Ala Lys . 35

Asn His Leu Pro Val Ser Ile Gly Val Ile Asn Lys Pro Gly Gly Gly 50

Gly Ala Ile Gly Leu Ser Glu Ile Ala Ala Ala Arg Pro Asn Gly Tyr 65

Lys Ile Gly Leu Gly Thr Val Glu Leu Thr Thr Leu Pro Ser Leu Gly 85

Met Val Arg Phe Lys Thr Ser Asp Phe Lys Pro Ile Ala Arg Leu Asn 100

Ala Asp Pro Ala Ala Ile Thr Val Arg Ala Asp Ala Pro Trp Asn Ser 115 120 125

Tyr Glu Glu Phe Met Ala Tyr Ser Lys Ala Asn Pro Gly Lys Val Arg 130 135 140

Ile Gly Asn Ser Gly Thr Gly Ala Ile Trp His Leu Ala Ala Ala 145 150 155 160

Leu Glu Asp Lys Thr Gly Thr Lys Phe Ser His Val Pro Tyr Asp Gly
165 170 175

Ala Ala Pro Ala Ile Thr Gly Leu Leu Gly Gly His Ile Glu Ala Val 180 185 190

Ser Val Ser Pro Gly Glu Val Ile Asn His Val Asn Gly Gly Lys Leu 195 200 205

Lys Thr Leu Val Val Met Ala Asp Glu Arg Met Lys Thr Met Pro Asp 210 215 220

Val Pro Thr Leu Lys Glu Lys Gly Val Asp Leu Ser Ile Gly Thr Trp 225 230 235 240

Arg Gly Leu Ile Val Ser Gln Lys Thr Pro Gln Asp Val Val Asp Val 245 250 255

Leu Ala Lys Ala Ala Lys Glu Thr Ala Glu Glu Pro Ala Phe Gln Asp 260 265 270

Ala Leu Gln Lys Leu Asn Leu Asn Tyr Ala Trp Leu Asp Ala Ala Ser 275 280 285

Phe Gln Thr Gln Ile Ser Glu Gln Glu Lys Tyr Phe Asp Glu Leu Leu 290 295 300

Thr Arg Leu Gly Leu Lys Lys 305 310

<210> 31

<211> 722

<212> PRT

<213> Escherichia coli

<400> 31

Met Leu Arg Trp Lys Arg Cys Ile Ile Leu Thr Phe Ile Ser Gly Ala 1 5 10 15

Ala Phe Ala Ala Pro Glu Ile Asn Val Lys Gln Asn Glu Ser Leu Pro 20 25 30

Asp Leu Gly Ser Gln Ala Ala Gln Gln Asp Glu Gln Thr Asn Lys Gly 35 40 45

Lys Ser Leu Lys Glu Arg Gly Ala Asp Tyr Val Ile Asn Ser Ala Thr 50 55 60

Gln Gly Phe Glu Asn Leu Thr Pro Glu Ala Leu Glu Ser Gln Ala Arg 65 70 75 80

Ser Tyr Leu Gln Ser Gln Ile Thr Ser Thr Ala Gln Ser Tyr Ile Glu 85 90 95

Asp Thr Leu Ser Pro Tyr Gly Lys Val Arg Leu Asn Leu Ser Ile Gly
100 105 110

Gln Gly Gly Asp Leu Asp Gly Ser Ser Ile Asp Tyr Phe Val Pro Trp 115 120 125

Tyr Asp Asn Gln Thr Thr Val Tyr Phe Ser Gln Phe Ser Ala Gln Arg

Lys Glu Asp Arg Thr Ile Gly Asn Ile Gly Leu Gly Val Arg Tyr Asn 145 150 155 160

Phe Asp Lys Tyr Leu Leu Gly Gly Asn Ile Phe Tyr Asp Tyr Asp Phe 165 170 175

Thr Arg Gly His Arg Arg Leu Gly Leu Gly Ala Glu Ala Trp Thr Asp
180 185 190

Tyr Leu Lys Phe Ser Gly Asn Tyr Tyr His Pro Leu Ser Asp Trp Lys

Asp Ser Glu Asp Phe Asp Phe Tyr Glu Glu Arg Pro Ala Arg Gly Trp 210 215 220

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Asp	Ile	Arg	Ala	Glu	Val	Trp	Leu	Pro	Ser	Tyr	Pro	Gln	Len	Glv	Glv
225					230	-				235			204	O ₁	240

Lys Ile Val Phe Glu Gln Tyr Tyr Gly Asp Glu Val Ala Leu Phe Gly 245 250 255

Thr Asp Asn Leu Glu Lys Asp Pro Tyr Ala Val Thr Leu Gly Leu Asn 260 265 270

Tyr Gln Pro Val Pro Leu Leu Thr Val Gly Thr Asp Tyr Lys Ala Gly 275 280 285

Thr Gly Asp Asn Ser Asp Val Ser Ile Asn Ala Thr Leu Asn Tyr Gln 290 295 300

Phe Gly Val Pro Leu Lys Asp Gln Leu Asp Ser Asp Lys Val Lys Ala 305 310 315 320

Ala His Ser Leu Met Gly Ser Arg Leu Asp Phe Val Glu Arg Asn Asn 325. 330 335

Phe Ile Val Leu Glu Tyr Lys Glu Lys Asp Pro Leu Asp Val Thr Leu 340 345 350

Trp Leu Lys Ala Asp Ala Thr Asn Glu His Pro Glu Cys Val Ile Lys 355 360 365

Asp Thr Pro Glu Ala Ala Val Gly Leu Glu Lys Cys Lys Trp Thr Ile 370 380

Asn Ala Leu Ile Asn His His Tyr Lys Ile Val Ala Ala Ser Trp Gln 385 390 395 400

Ala Lys Asn Asn Ala Ala Arg Thr Leu Val Met Pro Val Ile Lys Glu
405 410 415

Asn Thr Leu Thr Glu Gly Asn Asn Asn His Trp Asn Leu Val Leu Pro 420 425 430

Ala Trp Gln Tyr Ser Ser Asp Gln Ala Glu Gln Glu Lys Leu Asn Thr 435 440 445

(...

- Trp Arg Val Arg Leu Ala Leu Glu Asp Glu Lys Gly Asn Arg Gln Asn 455
- Ser Gly Val Val Glu Ile Thr Val Gln Gln Asp Arg Lys Ile Glu Leu 475
- Ile Val Asn Asn Ile Ala Asn Pro Glu Glu Asn Asn His Ser His Glu
- Ala Ser Ala Gln Ala Asp Gly Val Asp Gly Val Val Met Asp Leu Asp 505
- Val Thr Asp Ser Phe Gly Asp Asn Thr Asp Arg Asn Gly Asp Ala Leu 515
- Pro Glu Asp Asn Leu Thr Pro Gln Leu Tyr Asp Ala Gln Asp Lys Arg 535
- Val Thr Leu Thr Asn Lys Pro Cys Ser Thr Asp Asn Pro Cys Val Phe 550 555
- Ile Ala Lys Gln Asp Lys Glu Lys Gly Thr Val Thr Leu Ser Ser Thr 565 570
- Leu Pro Gly Thr Tyr Arg Trp Lys Ala Lys Ala Ala Pro Tyr Asp Asp 580 590
- Ser Asn Tyr Val Asp Val Thr Phe Leu Gly Ala Glu Ile Gly Gly Leu 595
- Asn Ala Phe Ile Tyr Arg Val Gly Ala Ala Lys Pro Ser Asn Leu Ile 610 615
- Gly Lys Asp Lys Glu Pro Leu Pro Ser Thr Thr Phe Ile Asp Leu Phe 630
- Tyr Gly Ala Thr Thr Ile Lys Thr Val Ser Ser Ser Arg Ser Lys Asn 645
- Leu Thr Lys Arg Trp Cys Ser Thr Thr Thr Ser Gly Asn Leu Pro Ala 660 665

Arg Ala Ser Met Val Ser Gly Cys Thr Gly Glu His Ser Asn Glu Asp 675 680 685

Ile Val Ile Pro Ala Thr Asn Arg Glu Ala Ala Gln Thr Tyr Gly Ala 690 695 700

Gln Ala Gly Asp Gly Leu Gln Gly Tyr Gly Leu Arg Val Leu Tyr Thr 705 710 715 720

Lys Lys

<210> 32

<211> 319

<212> PRT

<213> Escherichia coli

<400> 32

Met Lys Gln Asp Lys Arg Arg Gly Leu Thr Arg Ile Ala Leu Ala Leu 1 5 10 15

Ala Leu Ala Gly Tyr Cys Val Ala Pro Val Ala Leu Ala Glu Asp Ser 20 25 30

Ala Trp Val Asp Ser Gly Glu Thr Asn Ile Phe Gln Gly Thr Ile Pro 35 40 45

Trp Leu Tyr Ser Glu Gly Gly Ser Ala Thr Thr Asp Ala Asp Arg Val 50 55 60

Thr Leu Thr Ser Asp Leu Lys Gly Ala Arg Pro Gln Gly Met Lys Arg 65 70 75 80

Thr Ser Val Phe Thr Arg Val Ile Asn Ile Gly Asp Thr Glu Gly Asp 85 90 95

Val Asp Leu Gly Gly Leu Gly Asp Asn Ala Lys Thr Ile Asp Thr Ile
100 105 110

Arg Trp Met Ser Tyr Lys Asp Ala Gln Gly Gly Asp Pro Lys Glu Leu 115 120 125

Ala Thr Lys Val Thr Ser Tyr Thr Leu Thr Asp Ala Asp Arg Gly Arg 130 135 140

Tyr	Ile	Gly	Ile	Glu	Ile	Thr	Pro	Thr	Thr	Gln	Thr	Glv	Thr	Pro	Asn
145					150					155		4			160

- Val Gly Thr Ala Leu His Leu Tyr Asp Val Ser Thr Ala Ser Gly Gly
- Gly Ser Asp Ser Asp Asn Val Ala Pro Gly Pro Val Val Asn Gln Asn 180
- Leu Lys Val Ala Ile Phe Val Asp Gly Thr Ser Ile Asn Leu Ile Asn 195 200
- Gly Ser Thr Pro Ile Glu Leu Gly Lys Thr Tyr Val Ala Lys Leu Tyr 210
- Ser Asp Glu Asn Lys Asn Gly Lys Phe Asp Ala Gly Thr Asp Ala Asp 235
- Val Thr Ala Asn Tyr Asp Phe Arg Trp Val Leu Ser Gly Ser Ser Gln 245
- Gln Leu Gly Thr Ser Gly Gly Ile Val Asn Ser Ser Phe Asp Asn Asn 260
- Asn Leu Val Ile Pro Ala Thr Asn Asp Glu Ala Arg Thr Asn Leu Asn 275 280
- Gly Pro Ala Arg Asp Gly Lys Glu Ala Leu Ser Ile Pro Thr Asn Gly 295
- Asp Gly Val Gln Gly Tyr Lys Leu His Ile Ile Tyr Lys His Lys 310 315
- <210> 33
- <211> 629
- <212> PRT <213> Escherichia coli <400> 33
- Met Lys Lys Val Leu Thr Leu Ser Leu Leu Ala Leu Cys Val Ser His 5
- Ser Ala Val Ala Ala Asn Tyr Thr Phe Asn Asn Asp Asn Ile Ala Leu

Ser Phe Asp Asp Thr Asn Ser Thr Ile Val Leu Lys Asp Arg Arg Thr 35 40 45

Asn His Pro Ile Thr Pro Gln Glu Leu Phe Phe Leu Thr Leu Pro Asp 50 55 60

Glu Thr Lys Ile His Thr Ala Asp Phe Lys Ile Lys His Ile Lys Lys 65 70 75 80

Gln Asp Asn Ala Ile Val Ile Asp Phe Thr Arg Pro Asp Phe Asn Val 85 90 95

Thr Val Gln Leu Asn Leu Val Lys Gly Lys Tyr Ala Ser Ile Asp Tyr 100 105 110

Thr Ile Ala Ala Val Gly Gln Pro Arg Asp Val Ala Lys Ile Thr Phe 115 120 125

Phe Pro Thr Lys Lys Gln Phe Gln Ala Pro Tyr Val Asp Gly Ala Ile 130 135 140

Thr Ser Ser Pro Ile Ile Ala Asp Ser Phe Phe Ile Leu Pro Asn Lys 145 150 155 160

Pro Ile Val Asn Thr Tyr Ala Tyr Glu Ala Thr Thr Asn Leu Asn Val 165 170 175

Glu Leu Lys Thr Pro Ile Gln Pro Glu Thr Pro Val Ser Phe Thr Thr 180 185 190

Trp Phe Gly Thr Phe Pro Glu Thr Ser Gln Leu Arg Arg Ser Val Asn 195 200 . 205

Gln Phe Ile Asn Ala Val Arg Pro Arg Pro Tyr Lys Pro Tyr Leu His 210 215 220

Tyr Asn Ser Trp Met Asp Ile Gly Phe Phe Thr Pro Tyr Thr Glu Gln 225 230 235 240

Asp Val Leu Gly Arg Met Asp Glu Trp Asn Lys Glu Phe Ile Ser Gly. 245 250 255

 ϵ ...

- Arg Gly Val Ala Leu Asp Ala Phe Leu Leu Asp Asp Gly Trp Asp Asp 260 265 270
- Leu Thr Gly Arg Trp Leu Phe Gly Pro Ala Phe Ser Asn Gly Phe Ser 275 280 285
- Lys Val Arg Glu Lys Ala Asp Ser Leu His Ser Ser Val Gly Leu Trp
 290 295 300
- Leu Ser Pro Trp Gly Gly Tyr Asn Lys Pro Gln Arg Arg Ser Arg Phe 305 310 315 320
- Ala Cys Lys Arg Val Trp Val Arg Asn Arg Gly Arg Gln Ala Gly Ala 325 330 335
- Phe Gly Ser Glu Leu Leu Lys Asn Phe Asn Glu Gln Ile Ile Asn Leu 340 345 350
- Ile Lys Asn Glu His Ile Thr Ser Phe Lys Leu Asp Gly Met Gly Asn 355 360 365
- Ala Ser Ser His Ile Lys Gly Ser Pro Phe Ala Ser Asp Phe Asp Ala 370 380
- Ser Ile Ala Leu Leu His Asn Met Arg Arg Ala Asn Pro Asn Leu Phe 385 390 395 400
- Ile Asn Leu Thr Thr Gly Thr Asn Ala Ser Pro Ser Trp Leu Phe Tyr 405 410 415
- Ala Asp Ser Ile Trp Arg Gln Gly Asp Asp Ile Asn Leu Tyr Gly Pro 420 425 430
- Gly Thr Pro Val Gln Gln Trp Ile Thr Tyr Arg Asp Ala Glu Thr Tyr 435 440 445
- Arg Ser Ile Val Arg Lys Gly Pro Leu Phe Pro Leu Asn Ser Leu Met 450 455 460
- Tyr His Gly Ile Val Ser Ala Glu Asn Ala Tyr Tyr Gly Leu Glu Lys 465 470 475 480

Val Gln Thr Asp Ser Asp Phe Ala Asp Gln Val Trp Ser Tyr Phe Ala 485 490 495

Thr Gly Thr Gln Leu Gln Glu Leu Tyr Ile Thr Pro Ser Met Leu Asn 500 505 510

Lys Val Lys Trp Asp Thr Leu Ala Lys Ala Ala Lys Trp Ser Lys Glu 515 520 525

Asn Ala Ser Val Leu Val Asp Thr His Trp Ile Gly Gly Asp Pro Thr 530 540

Ala Leu Ala Val Tyr Gly Trp Ala Ser Trp Ser Lys Asp Lys Ala Ile 545 550 555 560

Leu Gly Leu Arg Asn Pro Ser Asp Lys Pro Gln Thr Tyr Tyr Leu Asp 565 570 575

Leu Ala Lys Asp Phe Glu Ile Pro Ala Gly Asn Ala Ala Gln Phe Ser 580 585 590

Leu Lys Ala Val Tyr Gly Ser Asn Lys Thr Val Pro Val Glu Tyr Lys 595 600 605

Asn Ala Thr Val Ile Thr Leu Gln Pro Leu Glu Thr Leu Val Phe Glu 610 620

Ala Val Thr Ile Asn 625

<210> 34

<211> 1778

<212> PRT

<213> Escherichia coli

<400> 34

Met Asn Lys Ile Phe Lys Val Ile Trp Asn Pro Ala Thr Gly Ser Tyr 1 5 10 15

Thr Val Ala Ser Glu Thr Ala Lys Ser Arg Gly Lys Lys Ser Gly Arg
20 25 30

Ser Lys Leu Leu Ile Ser Ala Leu Val Ala Gly Gly Leu Leu Ser Ser 35 40 45

Phe	Gly 50	Ala	Ser	Ala	Asp	Asn 55	Tyr	Thr	Gly	Gln	Pro 60	Thr	Asp	Tyr	Gly
Asp 65	Gly	Ser	Ala	Gly	Asp 70	Gly	Trp	Val	Ala	Ile 75	Gly	Lys	Gly	Ala	Ьу: 80
Ala	Asn	Thr	Phe	Met 85	Asn	Thr	Ser	Gly	Ala 90	Ser	Thr	Ala	Leu	Gly 95	туз
Asp	Ala	Ile	Ala 100	Glu	Gly	Glu	Tyr	Ser 105	Ser	Ala	Ile	Gly	Ser 110	Lys	Thi
Leu	Ala	Thr 115	Gly	Gly	Ala	Ser	Met 120	Ala	Phe	Gly	Val	Ser 125	Ala	Lys	Ala
Met	Gly 130	Asp	Arg	Ser	Val	Ala 135	Leu	Gly	Ala	Ser	Ser 140	Val	Ala	Asn	GlΣ
Asp 145	Arg	Ser	Met	Ala	Phe 150	Gly	Arg	Tyr	Ala	Lys 155	Thr	Asn	Gly	Phe	Thr 160
Ser	Leu	Ala	Ile	Gly 165	Asp	Ser	Ser	Leu	Ala 170	Asp	Gly	Glu	Lys	Thr 175	Ile
Ala	Leu	Gly	Asn 180	Thr	Ala	Lys	Ala	Tyr 185	Glu	Ile	Met	Ser	Ile 190	Ala	Leu
Зlу	Asp	Asn 195	Ala	Asn	Ala	Ser	Lys 200	Glu	Tyr	Ala	Met	Ala 205	Leu	Gly	Ala
Ser	Ser 210	Lys	Ala	Gly	Gly	Ala 215	Asp	Ser	Leu	Ala	Phe 220	Gly	Arg	Lys	Ser
Thr 225	Ala	Asn	Ser	Thr	Gly 230	Ser	Leu	Ala	Ile	Gly 235	Ala	Asp	Ser	Ser	Ser 240
Ser	Asn	Asp	Asn	Ala 245	Ile	Ala	Ile	Gly	Asn 250	Lys	Thr	Gln	Ala	Leu 255	Gly
/al	Asn	Ser	Met 260	Ala	Leu	Gly	Asn	Ala 265	Ser	Gln	Ala	Ser	Gly 270	Glu	Ser

- Ser Ile Ala Leu Gly Asn Thr Ser Glu Ala Ser Glu Gln Asn Ala Ile 275 280 285
- Ala Leu Gly Gln Gly Ser Ile Ala Ser Lys Val Asn Ser Ile Ala Leu 290 295 300
- Gly Ser Asn Ser Leu Ser Ser Gly Glu Asn Ala Ile Ala Leu Gly Glu 305 310 315 320
- Gly Ser Ala Ala Gly Gly Ser Asn Ser Leu Ala Phe Gly Ser Gln Ser 325 330 335
- Arg Ala Asn Gly Asn Asp Ser Val Ala Ile Gly Val Gly Ala Ala Ala 340 345 350
- Ala Thr Asp Asn Ser Val Ala Ile Gly Ala Gly Ser Thr Thr Asp Ala 355 360 365
- Ser Asn Thr Val Ser Val Gly Asn Ser Ala Thr Lys Arg Lys Ile Val 370 380
- Asn Met Ala Ala Gly Ala Ile Ser Asn Thr Ser Thr Asp Ala Ile Asn 385 390 395 400
- Gly Ser Gln Leu Tyr Thr Ile Ser Asp Ser Val Ala Lys Arg Leu Gly
 405 410 415
- Gly Gly Ala Thr Val Gly Ser Asp Gly Thr Val Thr Ala Val Ser Tyr
 420 425 430
- Ala Leu Arg Ser Gly Thr Tyr Asn Asn Val Gly Asp Ala Leu Ser Gly 435 440 445
- Ile Asp Asn Asn Thr Leu Gln Trp Asn Lys Thr Ala Gly Ala Phe Ser 450 455 460
- Ala Asn His Gly Ala Asn Ala Thr Asn Lys Ile Thr Asn Val Ala Lys
 465 470 475 480
- Gly Thr Val Ser Ala Thr Ser Thr Asp Val Val Asn Gly Ser Gln Leu 485 490 495
- Tyr Asp Leu Gln Gln Asp Ala Leu Leu Trp Asn Gly Thr Ala Phe Ser

500	505	510

- Ala Ala His Gly Thr Glu Ala Thr Ser Lys Ile Thr Asn Val Thr Ala 515 520 525
- Gly Asn Leu Thr Ala Gly Ser Thr Asp Ala Val Asn Gly Ser Gln Leu 530 540
- Lys Thr Thr Asn Asp Asn Val Thr Thr Asn Thr Thr Asn Ile Ala Thr 545 550 555 555
- Asn Thr Thr Asn Ile Thr Asn Leu Thr Asp Ala Val Asn Gly Leu Gly 565 570 575
- Asp Asp Ser Leu Leu Trp Asn Lys Ala Ala Gly Ala Phe Ser Ala Ala 580 585 590
- His Gly Thr Glu Ala Thr Ser Lys Ile Thr Asn Val Thr Ala Gly Asn 595 600 605
- Leu Thr Ala Gly Ser Thr Asp Ala Val Asn Gly Ser Gln Leu Lys Thr 610 615 620
- Thr Asn Asp Asn Val Thr Thr Asn Thr Thr Asn Ile Ala Thr Asn Thr 625 630 635 640
- Thr Asn Ile Thr Asn Leu Thr Asp Ala Val Asn Gly Leu Gly Asp Asp 645 650 655
- Ser Leu Leu Trp Asn Lys Thr Ala Gly Ala Phe Ser Ala Ala His Gly 660 665 670
- Thr Asp Ala Thr Ser Lys Ile Thr Asn Val Thr Ala Gly Asn Leu Thr 675 680 685
- Ala Gly Ser Thr Asp Ala Val Asn Gly Ser Gln Leu Lys Thr Thr Asn 690 695 700
- Asp Asn Val Thr Thr Asn Thr Thr Asn Ile Ala Thr Asn Thr Thr Asn 705 710 715 720
- Ile Thr Asn Leu Thr Asp Ala Val Asn Gly Leu Gly Asp Asp Ser Leu 725 730 735

- Leu Trp Asn Lys Thr Ala Gly Ala Phe Ser Ala Ala His Gly Thr Asp 740 745 750
- Ala Thr Ser Lys Ile Thr Asn Val Lys Ala Gly Asp Leu Thr Ala Gly 755 760 765
- Ser Thr Asp Ala Val Asn Gly Ser Gln Leu Lys Thr Thr Asn Asp Asn 770 775 780
- Val Ser Thr Asn Thr Thr Asn Ile Thr Asn Leu Thr Asp Ala Val Asn 785 790 795 800
- Gly Leu Gly Asp Asp Ser Leu Leu Trp Asn Lys Thr Ala Gly Ala Phe 805 810 815
- Ser Ala Ala His Gly Thr Asp Ala Thr Ser Lys Ile Thr Asn Val Lys 820 825 830
- Ala Gly Asp Leu Thr Ala Gly Ser Thr Asp Ala Val Asn Gly Ser Gln 835 840 845
- Leu Lys Thr Thr Asn Asp Asn Val Ser Thr Asn Thr Thr Asn Ile Thr 850 855 860
- Asn Leu Thr Asp Ser Val Gly Asp Leu Lys Asp Asp Ser Leu Leu Trp 865 870 875 880
- Asn Lys Ala Ala Gly Ala Phe Ser Ala Ala His Gly Thr Glu Ala Thr 885 890 895
- Ser Lys Ile Thr Asn Leu Leu Ala Gly Lys Ile Ser Ser Asn Ser Thr 900 905 910
- Asp Ala Ile Asn Gly Ser Gln Leu Tyr Gly Val Ala Asp Ser Phe Thr 915 920 925
- Ser Tyr Leu Gly Gly Gly Ala Asp Ile Ser Asp Thr Gly Val Leu Ser 930 935 940
- Gly Pro Thr Tyr Thr Ile Gly Gly Thr Asp Tyr Thr Asn Val Gly Asp 945 950 955 960

- Ala Leu Ala Ala Ile Asn Thr Ser Phe Ser Thr Ser Leu Gly Asp Ala 965 970 975
- Leu Leu Trp Asp Ala Thr Ala Gly Lys Phe Ser Ala Lys His Gly Ile 980 985 990
- Asn Asn Ala Pro Ser Val Ile Thr Asp Val Ala Asn Gly Ala Val Ser 995 1000 1005
- Ser Thr Ser Ser Asp Ala Ile Asn Gly Ser Gln Leu Tyr Gly Val 1010 1015 1020
- Ser Asp Tyr Ile Ala Asp Ala Leu Gly Gly Asn Ala Val Val Asn 1025 1030 1035
- Thr Asp Gly Ser Ile Thr Thr Pro Thr Tyr Ala Ile Ala Gly Gly 1040 1045 1050
- Ser Tyr Asn Asn Val Gly Asp Ala Leu Glu Ala Ile Asp Thr Thr 1055 1060 1065
- Leu Asp Asp Ala Leu Leu Trp Asp Thr Thr Ala Asn Gly Gly Asn 1070 1075 1080
- Gly Ala Phe Ser Ala Ala His Gly Lys Asp Lys Thr Ala Ser Val 1085 1090 1095
- Ile Thr Asn Val Ala Asn Gly Ala Val Ser Ala Thr Ser Asn Asp 1100 1105 1110
- Ala Ile Asn Gly Ser Gln Leu Tyr Ser Thr Asn Lys Tyr Ile Ala 1115 1120 1125
- Asp Ala Leu Gly Gly Asp Ala Glu Val Asn Ala Asp Gly Thr Ile 1130 1140
- Thr Ala Pro Thr Tyr Thr Ile Ala Asn Thr Asp Tyr Asn Asn Val 1145
- Gly Glu Ala Leu Asp Ala Leu Asp Asn Asn Ala Leu Leu Trp Asp 1160 1165 1170

Glu Asp Ala Gly Ala Tyr Asn Ala Ser His Asp Gly Asn Ala Ser 1175 1180 1185 Lys Ile Thr Asn Val Ala Ala Gly Asp Leu Ser Thr Thr Ser Thr 1195 1200 Asp Ala Val Asn Gly Ser Gln Leu Asn Ala Thr Asn Ile Leu Val 1210 Thr Gln Asn Ser Gln Met Ile Asn Gln Leu Ala Gly Asn Thr Ser 1220 1225 1230 Glu Thr Tyr Ile Glu Glu Asn Gly Ala Gly Ile Asn Tyr Val Arg Thr Asn Asp Ser Gly Leu Ala Phe Asn Asp Ala Ser Ala Ser Gly 1255 Ile Gly Ala Thr Ala Val Gly Tyr Asn Ala Val Ala Ser His Ala 1270 1275 Ser Ser Val Ala Ile Gly Gln Asp Ser Ile Ser Glu Val Asp Thr 1285 Gly Ile Ala Leu Gly Ser Ser Ser Val Ser Ser Arg Val Ile Val 1300 Lys Gly Thr Arg Asn Thr Ser Val Ser Glu Glu Gly Val Val Ile 1310 1315 Gly Tyr Asp Thr Thr Asp Gly Glu Leu Leu Gly Ala Leu Ser Ile 1330 Gly Asp Asp Gly Lys Tyr Arg Gln Ile Ile Asn Val Ala Asp Gly 1345 Ser Glu Ala His Asp Ala Val Thr Val Arg Gln Leu Gln Asn Ala 1360 1365 Ile Gly Ala Val Ala Thr Thr Pro Thr Lys Tyr Tyr His Ala Asn 1375

Ser Thr Ala Glu Asp Ser Leu Ala Val Gly Glu Asp Ser Leu Ala

	1385					1390					1395			
Met	Gly 1400	Ala	Lys	Thr	Ile	Val 1405		Gly	Asn	Ala	Gly 1410		Gly	Ile
Gly	Leu 1415	Asn	Thr	Leu	Val	Leu 1420		Asp	Ala	Ile	Asn 1425		Ile	Ala
Ile	Gly 1430	Ser	Asn	Ala	Arg	Ala 1435		His	Ala	Asp	Ser 1440		Ala	Met
Gly	Asn 1445	Gly	Ser	Gln	Thr	Thr 1450		Gly	Ala	Gln	Thr 1455	Asn	Tyr	Thr
Ala	Tyr 1460	Asn	Met	Asp	Ala	Pro 1465	Gln	Asn	Ser	Val	Gly 1470	Glu	Phe	Ser
Val	Gly 1475	Ser	Glu	Asp	Gly	Gln 1480	Arg	Gln	Ile	Thr	Asn 1485	Val	Ala	Ala
Gly	Ser 1490	Ala	Asp	Thr	Asp	Ala 1495	Val	Asn	Val	Gly	Gln 1500	Leu	Lys	Val
Thr	Asp 1505	Ala	Gln	Val	Ser	Gln 1510	Asn	Thr	Gln	Ser	Ile 1515	Thr	Asn	Leu
Asn	Thr 1520	Gln	Val	Thr	Asn	Leu 1525	Asp	Thr	Arg	Val	Thr 1530	Asn	Ile	Glu
Asn	Gly 1535	Ile	Gly	Asp	Ile	Val 1540	Thr	Thr	Gly	Ser	Thr 1545	Lys	Tyr	Phe
Lys	Thr 1550	Asn	Thr	Asp	Gly	Ala 1555	Asp	Ala	Asn	Ala	Gln 1360	Gly	Lys	Asp
Ser	Val 1565	Ala	Ile	Gly	Ser	Gly 1570	Ser	Ile	Ala	Ala	Ala 1575	Asp	Asn	Ser
Val	Ala 1580	Leu	Gly	Thr	Gly	Ser 1585	Val	Ala	Asp	Glu	Glu 1590	Asn	Thr	Ile
Ser	Val 1595	Gly	Ser	Ser	Thr	Asn 1600	Gln	Arg	Arg	Ile	Thr 1605	Asn	Val	Ala

Ala Gly Val Asn Ala Thr Asp Ala Val Asn Val Ser Gln Leu Lys 1610 1615 1620

Ser Ser Glu Ala Gly Gly Val Arg Tyr Asp Thr Lys Ala Asp Gly 1625 1630 1635

Ser Ile Asp Tyr Ser Asn Ile Thr Leu Gly Gly Gly Asn Ser Gly 1640 1650

Thr Thr Arg Ile Ser Asn Val Ser Ala Gly Val Asn Asn Asn Asp 1655 1660 1665

Ala Val Asn Tyr Ala Gln Leu Lys Gln Ser Val Gln Glu Thr Lys 1670 1680

Gln Tyr Thr Asp Gln Arg Met Val Glu Met Asp Asn Lys Leu Ser 1685 1690 1695

Lys Thr Glu Ser Lys Leu Ser Gly Gly Ile Ala Ser Ala Met Ala 1700 1705 1710

Met Thr Gly Leu Pro Gln Ala Tyr Thr Pro Gly Ala Ser Met Ala 1715 1720 1725

Ser Ile Gly Gly Gly Thr Tyr Asn Gly Glu Ser Ala Val Ala Leu 1730 1740

Gly Val Ser Met Val Ser Ala Asn Gly Arg Trp Val Tyr Lys Leu 1745 1750 1755

Gln Gly Ser Thr Asn Ser Gln Gly Glu Tyr Ser Ala Ala Leu Gly 1760 1765 1770

Ala Gly Ile Gln Trp 1775

<210> 35

(in ;

<211> 227

<212> PRT

<213> Escherichia coli

<400> 35

Met Asn Leu Lys Lys Thr Leu Leu Ser Val Leu Met Ile Leu Gln Leu

1				5					10					15	
Cys	Leu	Leu	Val 20	Gly	Cys	Asp	Tyr	Ile 25	Glu	. Lys	Ala	Ser	Lys 30	Val	Asp
Asp	Leu	Val 35	Thr	Gln	Gln	Glu	Leu 40	Gln	Lys	Ser	Lys	Ile 45	Glu	Ala	Leu
Glu	Lys 50	Gln	Gln	Glu	Leu	Asp 55	Lys	Arg	Lys	Ile	Glu 60	His	Phe	Glu	Lys
Gln 65	Gln	Thr	Thr	Ile	Ile 70	Asn	Ser	Thr	Lys	Thr 75	Leu	Ala	Gly	Val	Val 80
Lys	Ala	Val	Lys	Asn 85	Lys	Gln	Asp	Glu	Phe 90	Val	Phe	Thr	Glu	Phe 95	Asn
Pro	Ala	Gln	Thr 100	Gln	Tyr	Phe	Ile	Leu 105	Asn	Asn	Gly	Ser	Val 110	Gly	Leu
Ala	Gly	Lys 115	Ile	Leu	Ser	Ile	Asp 120	Ala	Val	Glu	Asn	Gly 125	Ser	Val	Ile
Arg	Ile 130	Ser	Leu	Val	Asn	Leu 135	Leu	Ser	Val	Pro	Val 140	Ser	Asn	Met	Gly
Phe 145	Tyr	Ala	Thr	Trp	Gly 150	Gly	Glu	Lys	Pro	Thr 155	Asp	Ile	Asn	Ala	Leu 160
Ala	Lys	Trp	Gln	Gln 165	Leu	Leu	Phe	Ser	Thr 170	Ala	Met	Asn	Ser	Ser 175	Leu
Lys	Leu	Leu	Pro 180	Gly	Gln	Trp	Gln	A sp 185	Ile	Asn	Leu	Thr	Leu 190	Lys	Gly
Val	Ser	Pro 195	Asn	Asn	Leu	Lys	Tyr 200	Leu	Lys	Leu	Ala	Ile 205	Asn	Met	Ala
Asn	Ile 210	Gln	Phe	Asp	Arg	Leu 215	Gln	Pro	Ala	Glu	Ser 220	Pro	Gln	Arg	Lys

Asn Lys Lys 225

- <210> 36

- <211> 1109 <212> PRT <213> Escherichia coli <400> 36
- Met Lys Arg Val Val Arg Leu Leu Gly Val Gly Leu Leu Leu Val
- Val Leu Leu Ile Leu Phe Val Leu Ala Gln Thr Thr Pro Leu Ile
- Ser Ala Gln Asp Glu His Ala Val Trp Leu Arg Leu Leu Ile Thr Ala
- Ile Val Ile Cys Leu Leu Ser Met Cys Ile Phe Phe Leu Phe Ser Phe
- Arg Gln Asn Glu Ala Ser Thr Ile Ser Leu Tyr Ala Gln Pro Thr Asp 75
- Ile Lys Glu Ile Asn Thr Glu Gln Pro Asn Tyr Ala Ser Leu Leu Thr
- Ile Tyr Leu Arg Asp Arg Tyr Gly Pro Phe Trp Arg Arg Lys Val Arg 105
- Leu Leu Val Thr Gly Glu Pro Glu Gln Ala Glu Ala Ile Ala Pro
- Gly Leu Thr Gly Gln His Trp Leu Glu Gly Asp His Thr Val Leu Ile 130
- Tyr Gly Gly Arg Pro Thr Ala Glu Pro Asp Val Thr Leu Leu Thr Ala 145
- Leu Lys Lys Leu Arg Arg Ser Arg Pro Leu Asp Gly Ile Ile Trp Ala 165 170
- Leu Thr Glu Glu Gln Ser Arg Gln Thr Ala Gln Leu Asp Lys Gly Trp 180
- Arg Gly Leu Ile Asn Gly Gly Lys Arg Leu Gly Phe Gln Ala Pro Leu

		195					200					205			
Tyr	Leu 210	Trp	Gln	Val	Cys	Asp 215	Asp	Gly	Asp	Tyr	Gln 220	Thr	Gly	Arg	Pro
Leu 225	Gln	Ser	Val	Gly	Cys 230	Leu	Leu	Pro	Glu	Arg 235	Cys	Thr	Pro	Glu	Gln 240
Leu	Ala	Val	Met	Leu 245	Glu	Ala	Ala	Ala	Asp 250	Gly	Thr	Gly	His	Val 255	Ala
Ala	Thr	Asp	Arg 260	Tyr	Arg	Met	Phe	Ser 265	Ala	Ala	Ser	Gly	Ser 270	Tyr	Pro
Cys	Arg	Ala 275	Gly	Tyr	Cys	Ser	Leu 280	Ala	Asp	Arg	Pro	Glu 285	Thr	Ala	Ala
Gly	Arg 290	Arg	Arg	Ile	Phe	Phe 295	Pro	Ala	Pro	Ala	Arg 300	Pro	Asp	Val	Gln
Pro 305	Ala	Ala	Cys	Arg	Arg 310	Ala	Gly	Gly	Gln	His 315	Leu	Met	Gln	Trp	Leu 320
Pro	Ser	Pro	Val	Trp 325	Ala	Gly	Val	Thr	Val 330	Ile	Thr	Arg	Ala	Gly 335	Ala
Arg	Trp	Val	Phe 340	Leu	Trp	Leu	Arg	Thr 345	Ala	Leu	Met	Ser	Ala 350	Val	Cys
Val	Leu	Val 355	Ile	Trp	Gly	Ala	Gly 360	Met	Thr	Thr	Ser	Phe 365	Phe	Ala	Asn
Arg	Ala 370	Leu	Val	Gln	Glu	Thr 375	Gly	Пle	Gln	Thr	Ala 380	Arg	Ala	Leu	Asp
Thr 385	Arg	Leu	Pro	Leu	Ala 390	Glu	Gln	Leu	Val	Ala 395	Leu	His	Thr	Leu	Gln .400
Gly	Glu	Leu	Glu	Arg 405	Leu	Gln	Tyr	Arg	Ile 410	Arg	Glu	Gly	Ala	Pro 415	Trp
ryr	Gln	Arg	Phe 420	Gly	Leu	Glu	Arg	Asn 425	Gln	Gln	Leu	Leu	Ala	Ala	Ala

Phe Pro Gly Tyr Ala Gln Ala Ala Asn Arg Leu Val Arg Asp Val Ala 435 440 445

Val Asp His Leu Gln Gln Gln Leu Asn Ala Phe Val Ala Leu Pro Pro 450 455 460

Asn Ser Pro Gln Arg Thr Ala Thr Gly Glu Gln Arg Tyr Lys Gln Leu 465 470 475 480

Lys Ala Leu Leu Met Thr Ser Arg Pro Glu Lys Ala Asp Ala Ala Phe 485 490 495

Phe Ser Thr Thr Leu Met Ala Asp Gly Leu Arg Tyr Glu Asn Ile Pro 500 505 510

Glu Gly Val Arg Gln Ser Val Leu Pro Ser Leu Leu Thr Phe Trp Thr 515 520 525

Ala Asn Leu Pro Glu His Pro Gln Trp Lys Thr Ser Pro Pro Pro Glu 530 540

Leu Thr Gly Ala Val Arg Lys Ile Leu Leu Arg Gln Ile Gly Val Arg 545 550 555 560

Asn Ala Glu Asn Thr Leu Tyr Gln Asn Val Leu Gln Gln Val Ser Arg 565 570 575

Asn Tyr Ala Asp Met Thr Leu Ala Asp Met Thr Gly Asp Thr Leu Thr 580 590

Glu Ser Leu Phe Ser Thr Glu Gln Thr Val Pro Gly Met Phe Thr Arg 595 600 , 605

Gln Ala Trp Glu Gly Gln Val Arg Glu Ala Ile Glu Gln Val Val Thr 610 615 620

Ala Arg Arg Glu Glu Ile Asp Trp Val Leu Ser Asp Arg Gln Gln Asp 625 630 635 640

Thr Ser Ala Asp Ile Ser Pro Asp Thr Leu Arg Asn Arg Leu Thr Ser 645 650 655

- Arg Tyr Phe Thr Asp Phe Ala Gly Ser Trp Leu Ala Phe Leu Asn Ser 660 665 670
- Ile His Trp Lys Lys Glu Asp Ser Leu Ser Gly Ile Leu Asp Gln Leu 675 680 685
- Thr Leu Met Ala Asp Ala Arg Gln Ser Pro Leu Ile Ala Leu Thr Asp 690 695 700
- Thr Leu Ala Trp Gln Ala Ala Thr Gly Arg Glu Asn Arg Gly Leu Ser 705 710 715 720
- Asp Ser Leu Ala Lys Ser Ala Gln Glu Leu Phe Asn Gly Lys Glu Lys 725 730 735
- Thr Pro Gln Gln Ser Arg Glu Gly Asp Asp Val Pro Val Gly Pro Leu 740 745 750
- Asp Lys Thr Phe Thr Pro Leu Leu Arg Leu Leu Gly Asp Lys Ala Gly 755 760 765
- Gly Gly Asp Ser Gln Leu Ser Leu Gln Thr Tyr Leu Thr Arg Val Thr 770 780
- Arg Val Arg Leu Lys Leu Gln Gln Val Thr Asn Ala Pro Asp Pro Gln 785 790 795 800
- Glu Met Thr Gln Gln Leu Ala Gln Thr Val Leu Gln Gly Lys Thr Val 805 810 815
- Asp Leu Thr Asp Thr Arg Asp Tyr Gly Arg Leu Ile Ala Ala Ser Leu 820 825 830
- Gly Glu Glu Trp Ser Gly Phe Gly Gln Ala Leu Phe Val Arg Pro Val 835 840 845
- Glu Gln Ser Trp Arg Gln Val Leu Thr Pro Ala Ala Asp Ser Leu Asn 850 855 860
- Arg Gln Trp Gln Arg Ala Ile Val Ser His Trp Asn Gln Asp Phe Ala 865 870 875 880

- Gly Arg Tyr Pro Phe Lys Ala Ser Gln Asn Asp Ala Ser Leu Pro Leu 885 890 895
- Leu Ala Gln Tyr Leu Arg Asp Asp Gly Arg Ile Asn Leu Phe Ile Ala 900 905 910
- Ala Asn Leu Ser Gly Val Leu Lys Arg Glu Gly Arg Tyr Trp Val Ala 915 920 925
- Asp Ala Met Asn Thr Gln Gly Leu Thr Val Asn Pro Asp Phe Ile Arg 930 935 940
- Ala Leu Asn Arg Leu Arg Asp Val Ala Asp Thr Ala Phe Ala Ser Gly 945 950 955 960
- Asp Ala Gly Ile His Phe Glu Leu Arg Ala Lys Pro Ala Arg Asp Val 965 970 975
- Met Lys Thr His Leu Val Ile Asp Gly Gln Glu Leu Glu Tyr Phe Asn 980 985 990
- Gln Lys Glu Arg Trp Gln Arg Phe Asn Trp Pro Asp Glu Gln Trp Gln
 995 1000 1005
- Pro Gly Ala Ser Leu Ser Trp Thr Ser Thr Gln Ala Met Glu Arg 1010 1015 1020
- Ile Leu Ala Asp Tyr Arg Gly Ser Trp Ser Leu Ile Arg Leu Leu 1025 1030 1035
- Glu Gln Ala Gln Val Thr Pro Val Asp Ser Ser Thr Phe Lys Val 1040 1045 1050
- Val Trp Lys Ala Gln Asp Gly Leu Pro Leu Asn Tyr Leu Leu Arg 1055 1060 1065
- Val Glu Gln Gly Lys Gly Pro Leu Ala Leu Leu Glu Leu Lys Asn 1070 1080
- Phe Arg Leu Pro Gly Gln Val Phe Leu Thr Gly Lys Ser Met Lys 1085 1090 1095
- Asp Val Glu Glu Tyr Gly Glu Asp Ala Asp Glu

1100 1105

<210> 37

<211> 178

<212> PRT

<213> Escherichia coli

<400> 37

Met Phe Pro Ile Arg Phe Lys Arg Pro Ala Leu Leu Cys Met Ala Met 1 5 10 15

Leu Thr Val Val Leu Ser Gly Cys Gly Leu Ile Gln Lys Val Val Asp 20 25 30

Glu Ser Lys Ser Val Ala Ser Ala Val Phe Tyr Lys Gln Ile Lys Ile 35 40 45

Leu His Leu Asp Phe Phe Ser Arg Ser Ala Leu Asn Thr Asp Ala Glu 50 55 60

Asp Thr Pro Leu Ser Thr Met Val His Val Trp Gln Leu Lys Thr Arg 65 70 75 80

Glu Asp Phe Asp Lys Ala Asp Tyr Asp Thr Leu Phe Met Gln Glu Glu 85 90 95

Lys Thr Leu Glu Lys Asp Val Leu Ala Lys His Thr Val Trp Val Lys

Pro Glu Gly Thr Ala Ser Leu Asn Val Pro Leu Asp Lys Glu Thr Gln 115 120 125

Phe Val Ala Ile Ile Gly Gln Phe Tyr His Pro Asp Glu Lys Ser Asp 130 135 140

Ser Trp Arg Leu Val Ile Lys Arg Asp Glu Leu Glu Ala Asp Lys Pro 145 150 155 160

Arg Ser Ile Glu Leu Met Arg Ser Asp Leu Arg Leu Leu Pro Leu Lys 165 170 175

Asp Lys

DODTARESAS I.

- <210> 38
- <211> 280
- <212> PRT
- <213> Escherichia coli
- <400> 38

Met Ile Ser Gly Gly Asn Met Leu Lys Glu Trp Met Ile Phe Thr Cys
1 10 15

Ser Leu Leu Thr Leu Ala Gly Ala Ser Leu Pro Leu Ser Gly Cys Ile 20 25 30

Ser Arg Gly Gln Glu Ser Ile Ser Glu Gly Ala Ala Phe Gly Ala Gly 35 40 45

Ile Leu Arg Glu Pro Gly Ala Thr Lys Lys Ala Asp Thr Lys Asp Leu 50 55 60

Asn Val Pro Pro Pro Val Tyr Gly Pro Pro Gln Val Ile Phe Arg Ile 65 70 75 80

Asp Asp Asn Arg Tyr Phe Thr Leu Glu Asn Tyr Thr His Cys Glu Asn 85 90 95

Gly Gln Thr Phe Tyr Asn Asn Lys Ala Lys Asn Ile His Val Lys Ile 100 105 110

Leu Asp Ala Ser Gly Tyr Leu Phe Lys Gly Arg Leu Phe Trp Leu Ser 115 120 125

Thr Arg Asp Asp Phe Leu Ala Phe Pro Ala Thr Leu Asn Thr Arg His

Thr Thr Asp Gly Gly Lys Arg Arg Ser Gly Val Pro Tyr Gly Ser Tyr
165 170 175

Thr Gln Asn Pro Thr Gly Ala Thr Arg Asp Tyr Asp Met Leu Val Met 180 185 190

Asn Asp Gly Phe Tyr Leu Leu Arg Tyr Arg Gly Gly Gln Gly Arg Phe
195 200 205

Ser Pro Val Ile Leu Arg Trp Ile Leu Ser Thr Glu Asp Ser Ser Gly 210 215 220

Val Val Arg Ser Glu Asp Ala Tyr Glu Leu Phe Arg Pro Gly Glu Glu 225 230 235 240

Val Pro Ser Thr Gly Phe Tyr Lys Ile Asp Leu Ser Arg Phe Tyr Pro

Lys Asn Asn Val Met Glu Met Gln Cys Asp Arg Thr Leu Glu Pro Val

Gln Pro Ser Glu Ser Lys Ile Gln 275 280

<210> 39

<211> 501

<212> PRT

<213> Escherichia coli

<400> 39

Met Glu His Val Ser Ile Lys Thr Leu Tyr His Leu Leu Cys Cys Met 1 5 10 15

Leu Leu Phe Ile Ser Ala Met Cys Ala Leu Ala Gln Glu His Glu Pro
20 25 30

Ile Gly Ala Gln Asp Glu Arg Leu Ser Thr Leu Ile His Gln Arg Met 35 40 45

Gln Glu Ala Lys Val Pro Ala Leu Ser Val Ser Val Thr Ile Lys Gly 50 55 60

Val Arg Gln Arg Phe Val Tyr Gly Val Ala Asp Val Ala Ser Gln Lys 70 75 80

Ala Asn Thr Leu Asp Thr Val Tyr Glu Leu Gly Ser Met Ser Lys Ala 85 90 95

Phe Thr Gly Leu Val Val Gln Ile Leu Ile Gln Glu Gly Arg Leu Arg

Gln Gly Asp Asp Ile Ile Thr Tyr Leu Pro Glu Met Arg Leu Asn Tyr 115 120 125

- Gln Gly Lys Pro Ala Ser Leu Thr Val Ala Asp Phe Leu Tyr His Thr 130 135 140
- Ser Gly Leu Pro Phe Ser Thr Leu Ala Arg Leu Glu Asn Pro Met Pro 145 150 155 160
- Gly Ser Ala Val Ala Gln Gln Leu Arg Asn Glu Asn Leu Leu Phe Ala 165 170 175
- Pro Gly Ala Lys Phe Ser Tyr Ala Ser Ala Asn Tyr Asp Val Leu Gly 180 185 190
- Ala Val Ile Glu Asn Val Thr Gly Lys Thr Phe Thr Glu Val Ile Ala 195 200 205
- Glu Arg Leu Thr Gln Pro Leu Gly Met Ser Ala Thr Val Ala Val Lys 210 215 220
- Gly Asp Glu Ile Ile Val Asn Lys Ala Ser Gly Tyr Lys Leu Gly Phe 225 230 235 240
- Gly Lys Pro Val Leu Phe His Ala Pro Leu Ala Arg Asn His Val Pro 245 250 255
- Ala Ala Tyr Ile His Ser Thr Leu Pro Asp Met Glu Ile Trp Ile Asp
 260 265 270
- Ala Trp Leu His Arg Lys Ala Leu Pro Ala Thr Leu Arg Glu Ala Met 275 280 285
- Ser Asn Ser Trp Arg Gly Asn Ser Asp Val Pro Leu Ala Ala Asp Asn 290 295 , 300
- Arg Ile Leu Tyr Ala Ser Gly Trp Phe Ile Asp Gln Asn Gln Gly Pro 305 310 315 320
- Tyr Ile Ser His Gly Gly Gln Asn Pro Asn Phe Ser Ser Cys Ile Ala 325 330 335
- Leu Arg Pro Asp Gln Gln Ile Gly Ile Val Ala Leu Ala Asn Met Asn 340 345 350

- Ser Asn Leu Ile Leu Gln Leu Cys Ala Asp Ile Asp Asn Tyr Leu Arg 355 360 365
- Ile Gly Lys Tyr Ala Asp Gly Ala Gly Asp Ala Ile Thr Ala Thr Asp 370 375 380
- Thr Leu Phe Val Tyr Leu Thr Leu Leu Leu Cys Phe Trp Gly Ala Val 385 390 395 400
- Val Val Val Arg Gly Ala Phe Arg Val Tyr Arg Ala Thr Ala His Gly
 405 410 415
- Pro Gly Lys Gln Gln Arg Leu Arg Leu Arg Val Arg Asp Tyr Ile Ile
 420 425 430
- Ala Leu Ala Val Pro Gly Leu Val Ala Ala Met Leu Tyr Val Ala Pro
 435 440 445
- Gly Ile Leu Ser Pro Gly Leu Asp Trp Arg Phe Ile Leu Val Trp Gly 450 455 460
- Pro Ser Ser Val Leu Ala Ile Pro Phe Gly Ile Ile Leu Leu Ala Phe 465 470 475 480
- Val Leu Thr Leu Asn His Gln Ile Lys Arg Ile Leu Leu His Asn Lys 485 490 495

Glu Trp Asp Asp Glu 500

- <210> 40
- <211> 682
- <212> PRT
- <213> Escherichia coli
- <400> 40

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- Met Lys Asn Lys Tyr Ile Ile Ala Pro Gly Ile Ala Val Met Cys Ser 1 10 15
- Ala Val Ile Ser Ser Gly Tyr Ala Ser Ser Asp Lys Lys Glu Asp Thr
- Leu Val Val Thr Ala Ser Gly Phe Thr Gln Gln Leu Arg Asn Ala Pro
 35 40 45

- Ala Ser Val Ser Val Ile Thr Ser Glu Gln Leu Gln Lys Lys Pro Val 50 60
- Ser Asp Leu Val Asp Ala Val Lys Asp Val Glu Gly Ile Ser Ile Thr 65 70 75 80
- Gly Gly Asn Glu Lys Pro Asp Ile Ser Ile Arg Gly Leu Ser Gly Asp 85 90 95
- Tyr Thr Leu Ile Leu Val Asp Gly Arg Arg Gln Ser Gly Arg Glu Ser
- Arg Pro Asn Gly Ser Gly Gly Phe Glu Ala Gly Phe Ile Pro Pro Val
- Glu Ala Ile Glu Arg Ile Glu Val Ile Arg Gly Pro Met Ser Ser Leu 130 135 140
- Tyr Gly Ser Asp Ala Ile Gly Gly Val Ile Asn Ile Ile Thr Lys Pro 145 150 155 160
- Val Asn Asn Gln Thr Trp Asp Gly Val Leu Gly Leu Gly Gly Ile Ile 165 170 175
- Gln Glu His Gly Lys Phe Gly Asn Ser Thr Thr Asn Asp Phe Tyr Leu 180 185 190
- Ser Gly Pro Leu Ile Lys Asp Lys Leu Gly Leu Gln Leu Tyr Gly Gly
 195 200 205
- Met Asn Tyr Arg Lys Glu Asp Ser Ile Ser Gln Gly Thr Pro Ala Lys 210 215 , 220
- Asp Asn Lys Asn Ile Thr Ala Thr Leu Gln Phe Thr Pro Thr Glu Ser 235 235
- Gln Lys Phe Val Phe Glu Tyr Gly Lys Asn Asn Gln Val His Thr Leu 245 250 255
- Thr Pro Gly Glu Ser Leu Asp Ala Trp Thr Met Arg Gly Asn Leu Lys
 260 265 270

- Gln Pro Asn Ser Lys Arg Glu Thr His Asn Ser Arg Ser His Trp Val 275
- Ala Ala Trp Asn Ala Gln Gly Glu Ile Leu His Pro Glu Ile Ala Val 290 295
- Tyr Gln Glu Lys Val Ile Arg Glu Val Lys Ser Gly Lys Lys Asp Lys 310
- Tyr Asn His Trp Asp Leu Asn Tyr Glu Ser Arg Lys Pro Glu Ile Thr 330
- Asn Thr Ile Ile Asp Ala Lys Val Thr Ala Phe Leu Pro Glu Asn Val
- Leu Thr Ile Gly Gly Gln Phe Gln His Ala Glu Leu Arg Asp Asp Ser 355
- Ala Thr Gly Lys Lys Thr Thr Glu Thr Gln Ser Val Ser Ile Lys Gln 370
- Lys Ala Val Phe Ile Glu Asn Glu Tyr Ala Ala Thr Asp Ser Leu Ala 390
- Leu Thr Gly Gly Leu Arg Leu Asp Asn His Glu Ile Tyr Gly Ser Tyr 410
- Trp Asn Pro Arg Leu Tyr Ala Val Tyr Asn Leu Thr Asp Asn Leu Thr 420 425
- Leu Lys Gly Gly Ile Ala Lys Ala Phe Arg Ala Pro Ser Ile Arg Glu
- Val Ser Pro Gly Phe Gly Thr Leu Thr Gln Gly Gly Ala Ser Ile Met 450 460
- Tyr Gly Asn Arg Asp Leu Lys Pro Glu Thr Ser Val Thr Glu Glu Ile 465
- Gly Ile Ile Tyr Ser Asn Asp Ser Gly Phe Ser Ala Ser Ala Thr Leu 485 490

Phe Asn Thr Asp Phe Lys Asn Lys Leu Thr Ser Tyr Asp Ile Gly Thr 505

Lys Asp Pro Val Thr Gly Leu Asn Thr Phe Ile Tyr Asp Asn Val Gly 515

Glu Ala Asn Ile Arg Gly Val Glu Leu Ala Thr Gln Ile Pro Val Tyr 535

Asp Lys Trp His Val Ser Ala Asn Tyr Thr Phe Thr Asp Ser Arg Arg

Lys Ser Asp Asp Glu Ser Leu Asn Gly Lys Ser Leu Lys Gly Glu Pro 570

Leu Glu Arg Thr Pro Arg His Ala Ala Asn Ala Lys Leu Glu Trp Asp 585

Tyr Thr Gln Asp Ile Thr Phe Tyr Ser Ser Leu Asn Tyr Thr Gly Lys

Gln Ile Trp Ala Ala Gln Arg Asn Gly Ala Lys Val Pro Arg Val Arg

Asn Gly Phe Thr Ser Met Asp Ile Gly Leu Asn Tyr Gln Ile Leu Pro 630

Asp Thr Leu Ile Asn Phe Ala Val Leu Asn Val Thr Asp Arg Lys Ser 650

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Arg Tyr Trp Ala Asn Val Arg Val Ser Phe 675

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Ile Gly Gly Tyr Lys Glu Arg Asn Ile Leu Met Leu Arg Ala Ile Lys 50

Lys Ile Ile Ile Met Thr Ile Val Asn Ile Ile Phe Phe Tyr Ser Phe

Gln Ser Thr Ala Asp Glu Met Val Leu Ile Lys Lys Tyr Gly Phe Gly 85

Leu Glu Arg Asp Ile Lys Gly Arg Pro Leu Ile Tyr Pro Ile Glu Asn 105

Tyr Asp Glu Cys Lys Lys Cys Asn His Met Asn Tyr Ile Ala Asp 120

Val Asn Ala Gln Leu Ala Met Ser Lys Lys Asn Asn Arg Ile Phe Ala 130

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Ser Tyr Cys Ala Ile Lys Thr Asn Gly Val Leu Gly Phe Ser Asn Arg

Lys Asp Val Leu Arg Glu Asn Gly Asp Ser Thr Gly Thr Thr Ser Ser 75

Ser Thr Asn Ala Met Met Leu Met Glu Asn Gly Glu Asn Glu Ile Ser

Leu Glu Ile Gly Ala Leu Arg Trp Phe Ser Asp Lys Pro Ala Ser Thr 105

Glu Glu Arg Gly His Phe Ser Gln Lys Ala Gly Cys Ser Leu Asp Leu

Val Arg Phe Val Lys Gln Glu Glu Thr Ile Leu Ser Ser Ile Lys Val 130 135

Thr Ile Asn Gln Gln Gly Ile Pro Glu Ala Gln Pro Asp Ser Met His 145 155

Pro Val Ile Arg Lys Glu Ile Leu Ala Glu Gln Ala Glu Pro Gly Phe 165

Ile Asp Pro Asp Tyr Phe Asn Glu Thr Tyr Phe Pro Lys Gly Met Lys 180 185

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Val Pro Val Val Asn Ile Ala Thr Pro Asn Gly Ala Gly Ile Ser His 50 55 60

Asn Arg Phe Thr Asp Tyr Asn Val Gly Lys Glu Gly Leu Ile Leu Asn 65 70 75 80

Asn Ala Thr Gly Lys Leu Asn Pro Thr Gln Leu Gly Gly Leu Ile Gln 85 90 95

Asn Asn Pro Asn Leu Lys Ala Gly Gly Glu Ala Lys Gly Ile Ile Asn 100 105 110

Glu Val Thr Gly Gly Lys Arg Ser Leu Leu Gln Gly Tyr Thr Glu Val

Ala Gly Lys Ala Ala Asn Val Met Val Ala Asn Pro Tyr Gly Ile Thr 130 135 140

Cys Asp Gly Cys Gly Phe Ile Asn Thr Pro His Ala Thr Leu Thr Thr 145 150 155 160

Gly Lys Pro Val Met Asn Ala Asp Gly Ser Leu Gln Ala Leu Glu Val 165 170 175

Thr Glu Gly Ser Ile Thr Ile Asn Gly Ala Gly Leu Asp Gly Thr Arg 180 185 190

Ser Asp Ala Val Ser Ile Ile Ala Arg Ala Thr Glu Val Asn Ala Ala 195 200 205

Leu His Ala Lys Asp Leu Thr Val Thr Ala Gly Ala Asn Arg Val Thr 210 215 220

Ala Asp Gly Arg Val Arg Ala Leu Lys Gly Glu Gly Asp Val Pro Lys 225 230 235 240

Val Ala Val Asp Thr Gly Ala Leu Gly Gly Met Tyr Ala Arg Ile 245 250 255

- His Leu Thr Ser Thr Glu Ser Gly Val Gly Val Asn Leu Gly Asn Leu 260 265 270
- Tyr Ala Arg Asp Gly Asp Ile Thr Leu Asp Ala Ser Gly Arg Leu Thr 275 280 285
- Val Asn Asn Ser Leu Ala Thr Gly Ala Val Thr Ala Lys Gly Gln Gly 290 295 300
- Val Thr Leu Thr Gly Asp His Lys Ala Gly Gly Asn Leu Ser Val Ser 305 310 315 320
- Ser Arg Arg Asp Ile Val Leu Ser Asn Gly Thr Leu Asn Ser Asp Lys 325 330 335
- Asp Leu Ser Leu Thr Ala Gly Gly Arg Ile Thr Gln Gln Asn Glu Lys 340 345 350
- Leu Thr Ala Gly Arg Asp Val Thr Leu Ala Ala Lys Asn Ile Thr Gln 355 360 365
- Asp Thr Ala Ser Gln Ile Asn Ala Ala Arg Asp Ile Val Thr Val Ala 370 380
- Ser Asp Thr Leu Thr Thr Gln Gly Gln Ile Thr Ala Gly Gln Asn Leu 385 390 395 400
- Thr Ala Ser Ala Thr Thr Leu Thr Gln Asp Gly Ile Leu Leu Ala Lys
 405 410 415
- Ser His Ala Gly Leu Asn Ala Gly Thr Leu Asn Asn Ser Gly Ala Val 420 425 430
- Gln Gly Ala Thr Leu Thr Leu Gly Ser Thr Thr Leu Ser Asn Ser Gly
 435 440 445
- Ser Leu Leu Ser Gly Gly Pro Leu Thr Met Asn Thr Arg Asp Phe Thr 450 455. 460
- Gln Ser Gly Arg Thr Gly Ala Lys Gly Lys Val Asp Ile Met Ala Ser 465 470 475 480

- Gly Lys Leu Thr Ser Thr Gly Leu Leu Val Thr Met His Leu Val Leu 485 490 495
- Lys Ala Gln Asp Val Thr Gln Asn Gly Val Leu Ser Gly Gly Lys Gly 500 505 510
- Leu Thr Val Ser Ala Thr Ser Ser Gly Lys Lys Ser Val Thr His Ser 515 520 525
- Asp Ala Ala Met Thr Leu Asn Val Thr Thr Val Ala Leu Asp Gly Glu 530 540
- Thr Ser Ala Gly Asp Thr Leu Arg Val Gln Ala Asp Lys Leu Ser Thr 545 550 555 560
- Ala Ala Gly Ala Gln Leu Gln Ser Gly Lys Asn Leu Ser Ile Asn Ala 565 570 575
- Arg Asp Ala Arg Leu Ala Gly Thr Gln Ala Ala Gln Gln Thr Met Val
- Val Asn Ala Ser Glu Lys Leu Thr His Ser Gly Lys Ser Ser Ala Pro
 595 600 605
- Ser Leu Ser Leu Ser Ala Pro Glu Leu Thr Ser Ser Gly Val Leu Val 610 615 620
- Gly Ser Ala Leu Asn Thr Gln Ser Gln Thr Leu Thr Asn Ser Gly Leu 625 630 635 640
- Leu Gln Gly Glu Ala Ser Leu Thr Val Asn Thr Gln Arg Leu Asp Asn 645 650 655
- Gln Gln Asn Gly Thr Leu Tyr Ser Ala Ala Asp Leu Thr Leu Asp Ile 660 665 670
- Pro Asp Ile Arg Asn Ser Gly Leu Ile Thr Gly Asp Asn Gly Leu Met 675 680 685
- Leu Asn Ala Val Ser Leu Ser Asn Pro Gly Lys Ile Ile Ala Asp Thr 690 695 700

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- Leu Ser Val Arg Ala Thr Thr Leu Asp Gly Asp Gly Leu Leu Gln Gly 705 710 715 720
- Ala Gly Ala Leu Ala Leu Ala Gly Asp Thr Leu Ser Gln Gly Ser His 725 730 735
- Gly Arg Trp Leu Thr Ala Asp Asp Leu Ser Leu Arg Gly Lys Thr Leu 740 745 750
- Asn Thr Ala Gly Thr Thr Gln Gly Gln Asn Ile Thr Val Gln Ala Asp 755 760 765
- Arg Trp Ala Asn Ser Gly Ser Val Leu Ala Thr Gly Asn Leu Thr Ala 770 780
- Ser Ala Thr Gly Gln Leu Thr Ser Thr Gly Asp Ile Met Ser Gln Gly 785 790 795 800
- Asp Thr Thr Leu Lys Ala Ala Thr Thr Asp Asn Arg Gly Ser Leu Leu 805 810 815
- Ser Ala Gly Thr Leu Ser Leu Asp Gly Asn Ser Leu Asp Asn Arg Gly 820 825 830
- Thr Val Gln Gly Asn His Val Thr Ile Arg Gln Asn Ser Val Thr Asn 835 840 845
- Ser Gly Thr Leu Thr Gly Ile Ala Ala Leu Thr Leu Ala Ala Arg Met 850 855 860
- Ala Ser Pro Gln Pro Ala Leu Met Asn Asn Gly Gly Ser Leu Leu Thr 865 870 875 880
- Ser Gly Asp Leu Thr Ile Thr Ala Gly Ser Ile Thr Ser Ser Gly His 885 890 895
- Trp Gln Gly Lys Arg Val Leu Ile Thr Ala Asp Ser Leu Ala Asn Ser 900 905 910
- Gly Ala Ile Gln Ala Ala Asp Ser Leu Thr Ala Arg Leu Thr Gly Glu 915 920 925
- Leu Val Ser Thr Ala Gly Ser Lys Val Thr Ser Asn Gly Glu Met Ala

930 935 940

Leu Ser Ala Leu Asn Leu Ser Asn Ser Gly Gln Trp Ile Ala Lys Asn 945 950 955 960

Leu Thr Leu Lys Ala Asn Ser Leu Thr Ser Ala Gly Asp Ile Thr Gly 965 970 975

Val Asp Thr Leu Thr Leu Thr Val Asn Gln Thr Leu Asn Asn Gln Ala 980 985 990

Asn Gly Lys Leu Leu Ser Ala Gly Val Leu Thr Leu Lys Ala Asp Ser 995 1000 1005

Val Thr Asn Asp Gly Gln Leu Gln Gly Asn Val Thr Thr Ile Thr 1010 1015 1020

Ala Gly Gln Leu Thr Asn Gly Gly His Leu Gln Gly Glu Thr Leu 1025 1030 1035

Thr Leu Thr Ala Ser Gly Gly Val Asn Asn Arg Ser Gly Gly Val 1040

Leu Met Ser Arg Asn Ala Leu Asn Val Ser Thr Ala Thr Leu Ser 1055

Asn Gln Ser Thr Ile Gln Gly Gly Gly Gly Val Ser Leu Asn Ala 1070 1080

Thr Asp Arg Leu Gln Asn Asp Gly Lys Ile Leu Ser Gly Ser Asn 1085 1090 1095

Leu Thr Leu Thr Ala Gln Val Leu Ala Asn Thr Gly Ser Gly Leu 1100 1110

Val Gln Ala Ala Thr Leu Leu Leu Asp Val Val Asn Thr Val Asn 1115 1120 1125

Gly Gly Arg Val Leu Ala Thr Gly Ser Asp Val Lys Gly Thr Thr

Leu Asn Asn Thr Gly Thr Leu Gln Gly Ala Thr Leu Val Asn Tyr 1145

おかいしつしい ときし

7777 EET 2

His	Thr 1160	Phe	e Sei	r Ser	Gly	7 Thr 1165	Leu	Leu	Gly	Thr	Ser 1170		/ Let	ı Gly
Val	Lys 1175	Gl ₃	/ Sei	c Ser	Leu	Leu 1180	Gln	Asn	. Gly	Thr	Gly 1185		j Lei	ı Tyr
Ser	Ala 1190	Gl ^y	⁄ Asr	ı Leu	Leu	Leu 1195	Asp	Ala	Gln	Asp	Phe 1200		Gly	/ Gln
Gly	Gln 1205	Val	. Val	. Ala	Thr	Gly 1210	Asp	Val	Thr	Leu	Lys 1215		ıIl∈	Ala
Ala	Leu 1220	Thr	Asn	. His	Gly	Thr 1225	Leu	Ala	Ala	Gly	Lys 1230		Leu	Ser
Val	Thr 1235	Ser	Gln	Asn	Ala	Ile 1240	Thr	Asn	Gly	Gly	Val 1245		Gln	Gly
Asp	Ala 1250	Met	Val	Leu	Gly	Ala 1255	Gly	Glu	Ala	Phe	Thr 1260	Asn	Asn	Gly
Leu	Thr 1265	Ala	Gly	Lys	Gly	Asn 1270	Ser	Val	Phe	Ser	Ala 1275	Gln	Arg	Leu
Phe	Leu 1280	Asn	Ala	Pro	Gly	Ser 1285	Leu	Gln	Gly	Gly	Gly 1290	Asp	Val	Ser
Leu	Asn 1295	Ser	Arg	Ser	Asp	Ile 1300	Thr	Ile	Ser	Gly	Phe 1305	Thr	Gly	Thr
Ala	Gly 1310	Ser	Leu	Thr	Met	Asn 1315	Val	Ala	Gly	Thr	Leu 1320	Leu	Asn	Ser
Ala	Leu 1325	Ile	Tyr	Ala	Gly	Asn 1330	Asn	Leu	Lys	Leu	Phe 1335	Thr	qaA	Arg
Leu :	His 1340	Asn	Gln	His	Gly	Asp 1345	Ile	Leu .	Ala		Asn 1350	Ser	Leu	Trp
Val (Gln 1355	Lys	Asp	Ala	Ser	Gly 1360	Gly :	Ala .	Asn '		Glu 1365	Ile	Ile	Asn

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Thr	Gly 1385	His	Leu	Leu	Asn	Gln 1390		Gİu	Gly	Phe	Ser 1395		Thr	Thr
Thr	Thr 1400	Arg	Thr	Asn	Pro	Ser 1405		Ile	Gln	Gly	Met 1410		Asn	Ala
Leu	Val 1415	Asp	Ile	Pro	Leu	ser 1420		Leu	Pro	Asp	Gly 1425	Ser	Tyr	Gly
Tyr	Phe 1430	Thr	Arg	Glu	Val	Glu 1435		Gln	His	Gly	Thr 1440	Pro	Cys	Asn
Gly	His 1445	Gly	Ala	Cys	Asn	Ile 1450		Met	qaA	Thr	Leu 1455	Tyr	Tyr	Tyr
Ala	Pro 1460	Phe	Ala	Asp	Ser	Ala 1465		Gln	Arg	Phe	Leu 1470	Ser	Ser	Gln
Asn	Ile 1475	Thr	Thr	Val	Thr	Gly 1480	Ala	Asp	Asn	Pro	Ala 1485	Gly	Arg	Ile
Ala	Ser 1490	Gly	Arg	Asn	Leu	Ser 1495	Ala	Glu	Ala	Glu	Arg 1500	Leu	Glu	Asn
Arg	Ala 1505	Ser	Phe	Ile	Leu	Ala 1510	Asn	Gly	Asp		Ala 1515	Leu	Ser	Gly
Arg	Glu 1520	Leu	Ser	Asn	Gln	Ser 1525	Trp	Gln	Thr	Gly	Thr 1530	Glu	Asn	Glu
Tyr	Leu 1535	Val	Tyr	Arg	Tyr	Asp 1540	Pro	Lys	Thr	Phe	Tyr 1545	Gly	Ser	Tyr
Ala	Thr 1550	Gly	Ser	Leu	Asp	Lys 1555	Leu	Pro	Leu	Leu	Ser 1560	Pro	Glu	Phe
Glu	Asn 1565	Asn	Thr	Ile		Phe 1570	Ser	Leu	Asp	Gly	Arg 1575	Glu	Lys	Asp

Tyr	Thr 1580		Gly	Lys	Thr	Tyr 1585		Ser	Val	Ile	Gln 1590		Gly	Gly
Asp	Val 1595		Thr	Arg	Phe	Thr 1600		Ser	Ile	Asn	Asn 1605		Thr	Thr
Thr	Ala 1610		Ala	Gly	Ser	Val 1615		Pro	Val	Val	Ser 1620	Ala	Pro	Val
Leu	Asn 1625	Thr	Leu	Ser	Gln	Gln 1630	Thr	Gly	Gly	Asp	Ser 1635	Leu	Thr	Gln
Thr	Ala 1640		Gln	Gln		Glu 1645		Val	Val	Val	Gly 1650	Ser	Pro	Gln
Trp	His 1655		Glu	Leu		Gly 1660	Ala	Leu	Lys	Asn	Ile 1665	Ala	Gly	Gly
Ser	Pro 1670	Leu	Thr	Gly	Gln	Thr 1675		Ile	Ser	Asp	Asp 1680	Trp	Pro	Leu
Pro	Ser 1685	Gly	Asn	Asn	Gly	Tyr 1690	Leu	Val	Pro		Thr 1695	Asp	Pro	Asp
Ser	Pro 1700	Tyr	Leu	Ile	Thr	Val 1705	Asn	Pro	Lys	Leu	Asp 1710	Gly	Leu	Gly
Gln	Val 1715	Asp	Ser	His	Leu	Phe 1720	Ala	Gly	Leu	Tyr	Glu 1725	Leu	Leu	Gly
Ala	Lys 1730	Pro	Gly	Gln	Ala	Pro 1735	Arg	Glu	Thr	Ala	Pro 1740	Ser	Tyr	Thr
Asp	Glu 1745	Lys	Gln	Phe	Leu	Gly 1750	Ser	Ser	Tyr	Phe	Leu 1755	Asp	Arg	Leu
Gly	Leu 1760	Lys	Pro	Glu	Lys	Asp 1765	Tyr	Arg	Phe	Leu	Gly 1770	Asp	Ala	Val
Phe	Asp 1775	Thr	Arg	Tyr	Val	Ser 1780	Asn	Ala	Val	Leu	Ser 1785	Arg	Thr	Gly
Ser	Arg	Tyr	Leu	Asn	Gly	Leu	Gly	Ser	Asp	Thr	Glu	Gln	Met	Arg

<u>(iii</u>

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Tyr	Leu 1805	Met	Asp	Asn	Ala	Ala 1810	Arg	Gln	Gln	Lys	Gly 1815	Leu	Gly	Leu
Glu	Phe 1820		Val	Ala	Leu	Thr 1825	Ala	Glu	Gln	Ile	Ala 1830	Gln	Leu	Asp
Gly	Ser 1835		Leu	Trp	Trp	Glu 1840	Ser	Val	Thr	Ile	Asn 1845	Gly	Gln	Thr
Val	Met 1850	Val	Pro	Lys	Leu	Tyr 1855	Leu	Ser	Pro	Glu	Asp 1860	Ile	Thr	Leu
His	Asn 1865	Gly	Ser	Val	Ile	Ser 1870	Gly	Asn	Asn	Val	Gln 1875	Leu	Ala	Gly
Gly	Asn 1880	Ile	Thr	Asn	Ser	Gly 1885	Gly	Ser	Ile	Asn	Ala 1890	Gln	Asn	Asp
Leu	Ser 1895	Leu	Asp	Ser	Ser	Gly 1900	Tyr	Ile	Asp	Asn	Leu 1905	Asn	Ala	Gly
Leu	Ile 1910	Ser	Ala	Gly	Gly	Ser 1915	Leu	Asp	Leu	Ser	Ala 1920	Ile	Gly	Asp
Ile	Ser 1925	Asn	Ile	Ser	Ser	Val 1930	Ile	Ser	Gly	Lys	Thr 1935	Val	Gln	Leu
Glu	Ser 1940	Val	Ser	Gly	Asn	Ile 1945	Ser	Asn	Ile	Thr	Arg 1950	Arg	Gln	Gln
Trp	Asn 1955	Ala	Gly	Ser	Asp	Ser 1960	Glņ	Tyr	Gly	Gly	Val 1965	His	Leu	Ser
Gly	Thr 1970	Asp	Thr	Gly	Pro	Val 1975	Ala	Thr	Ile	Lys	Gly 1980	Thr	Asp	Ser
Leu	Ser 1985	Leu	Asp	Ala	Gly	Lys 1990	Asn	Ile	Asp	Ile	Thr 1995	Gly	Ala	Thr
Val	Ser 2000	Ser	Gly	Gly	Asp	Leu 2005	Gly	Met	Ser	Ala	Gly 2010	Asn	Asp	Ile

Asn	Ile 2015	Ala	Ala	Asn	Leu	Ile 2020		Gly	Ser	Lys	Ser 2025		Ser	Gly
Phe	Trp 2030	His	Thr	Asp	Asp	Asn 2035		Ser	Ser	Ser	Thr 2040		Ser	Gln
Gly	Ser 2045	Ser	Ile	Ser	Ala	Gly 2050		Asn	Leu	Ala	Met 2055		Ala	Gly
His	Asn 2060	Leu	Asp	Val	Thr	Ala 2065	Ser	Ser	Val	Ser	Ala 2070		His	Ser
Ala	Leu 2075	Leu	Ser	Cys	Arg	Ser 2080	Arg	Pro	Ser	Leu	Glu 2085	Cys	Ser	Gln
Gly	Lys 2090	Ala	Lys	Thr	Ser	Arg 2095	Asn	Gly	Arg	Ser	Glu 2100	Ser	His	Glu
Ser	His 2105	Ala	Ala	Val	Ser	Thr 2110	Val	Thr	Ala	Gly	Asp 2115	Asn	Phe	Leu
Leu	Val 2120	Ala	Gly	Arg	Asp	Ile 2125	Ala	Ser	Gln		Ala 2130	Gly	Met	Ala
Ala	Glu 2135	Asn	Asn	Val	Val	Ile 2140	Arg	Gly	Gly		Asp 2145	Val	Asn	Leu
Val	Ala 2150	Glu	Ser	Ala	Gly	Ala 2155	Gly	Asp	Ser		Thr 2160	Ser	Lys	Lys
Lys	Lys 2165	Glu	Ile	Asn	Glu	Thr 2170	Val	Arg	Gln	Gln	Gly 2175	Thr	Glu	Ile
Ala	Ser 2180	Gly	Gly	Asp	Thr	Thr 2185	Val	Asn	Ala	Gly	Arg 2190	Asp	Ile	Thr
Ala	Val 2195	Ala	Ser	Ser	Val	Thr 2200	Ala	Thr	Gly	Asn	Ile 2205	Ser	Val	Asn
Ala	Gly 2210	Arg	Asp	Val	Ala	Leu 2215	Thr	Thr	Ala		Glu 2220	Ser	Asp	Tyr

His	Tyr 2225	Leu	ı Glu	ı Thr	Lys	Lys 2230	Lys	Ser	Gly	. Glà	Phe 2235		Ser	· Ly
Lys	Thr 2240	Thr	· Arc	Thr	: Ile	Ser 2245	Glu	Asp	Ser	Ala	Thr 2250		Glu	. Ala
Gly	Ser 2255	Leu	Leu	. Ser	Gly	Asn 2260	Arg	Val	Thr	Val	Asn 2265		Gly	Ası
Asn	Leu 2270	Thr	Val	Glu	Gly	Ser 2275	Asp	Val	Val	Ala	Asp 2280		Asp	Val
Ser	Leu 2285	Ala	Ala	Gly	Asn	His 2290	Val	Asp	Val	Leu	Ala 2295	Ala	Thr	Sei
Thr	Asp 2300	Thr	Ser	Trp	Arg	Phe 2305	Lys	Glu	Thr	Lys	Lys 2310		Gly	Leu
Met	Gly 2315	Thr	Gly	Gly	Ile	Gly 2320	Phe	Thr	Ile	Gly	Ser 2325		Lys	Thr
Thr	His 2330	Asp	Arg	Arg	Glu	Ala 2335	Gly	Thr	Thr	Gln	Ser 2340	Gln	Ser	Ala
Ser	Thr 2345	Ile	Gly	Ser	Thr	Ala 2350	Gly	Asn	Val	Ser	Ile 2355	Thr	Ala	Gly
Lys	Gln 2360	Ala	His	Ile	Ser	Gly 2365	Ser	Asp	Val	Ile	Ala 2370	Asn	Arg	Asp
Ile	Ser 2375	Ile	Thr	Gly	Asp	Ser 2380	Val	Val	Val	Asp	Pro 2385	Gly	His	Asp
Arg	Arg 2390	Thr	Val	Asp	Glu	Lys 2395	Phe	Glu	Gln	Lys	Lys 2400	Ser	Gly	Leu
Thr	Val 2405	Ala	Leu	Ser	Gly	Thr 2410	Val	Gly	Ser	Ala	Ile 2415	Asn	Asn	Ala
Val	Thr 2420	Ser	Ala	Gln	Glu	Thr 2425	Lys	Glu	Ser	Ser	Asp	Ser	Arg	Leu

Lys	Ala 2435	Leu	Gln	Ala	Thr	Lys 2440		Ala	Leu	Ser	Gly 2445	Val	Gln	Ala
Gly	Gln 2450	Ala	Ala	Thr	Met	Ala 2455		Ala	Thr	Gly	Asp 2460	Pro	Asn	Ala
Gly	Val 2465	Ser	Leu	Ser	Leu	Thr 2470	Thr	Gln	Lys	Ser	Lys 2475		Gln	Glr
His	Ser 2480	Glu	Ser	Asp	Thr	Val 2485	Ser	Gly	Ser	Thr	Leu 2490	Asn	Ala	Glλ
Asn	Asn 2495	Leu	Ser	Val	Val	Ala 2500	Thr	Gly	Lys	Asn	Arg 2505	Gly	Asp	Asr
Arg	Gly 2510	Asp	Ile	Val	Ile	Ala 2515	Gly	Ser	Gln	Leu	Lys 2520	Ala	Gly	Gly
Asn	Thr 2525	Ser	Leu	Asp	Ala	Ala 2530	Asn	Asp	Ile	Leu	Leu 2535	Ser	Gly	Ala
Ala	Asn 2540	Thr	Gln	Lys	Thr	Thr 2545	Gly	Arg	Asn	Ser	Ser 2550	Ser	Gly	Gly
Gly	Val 2555	Gly	Val	Ser	Ile	Gly 2560	Ala	Gly	Lys	Gly	Ala 2565	Gly	Ile	Ser
Ala	Phe 2570	Ala	Ser	Val	Asn	Ala 2575	Ala	Lys	Gly	Arg	Glu 2580	Lys	Gly	Asn
Gly	Thr 2585	Thr	Thr	Asp	Lys	Thr 2590	Val	Thr	Ile	Asn	Ser 2595	Gly	Arg	Asp
Thr	Val 2600	Leu	Asn	Gly	Ala	Gln 2605) Val	Asn	Gly	Asn	Arg 2610	Ile	Ile	Ala
Asp	Val 2615	Gly	His	Asp	Leu	Leu 2620	Ile	Ser	Ser	Gln	Gln 2625	Asp	Thr	Ser
Lys	Tyr 2630	qzA	Ser	Lys	Gln	Thr 2635	Ser	Val	Ala	Ala	Gly 2640	Gly	Ser	Phe

Thr Phe Gly Ser Met Thr Gly Ser Gly Tyr Ile Ala Ala Ser Arg

2645 2650 2655

Asp Lys Met Lys Ser Arg Phe Asp Ser Val Ala Glu Gln Thr Gly 2660 2665

Met Phe Ala Arg Val Met Val Ala Ser Thr Ser Gln Trp Val Asn 2675 2680

Ile Pro Asn Trp Met Val Arg Ser Leu Pro His Cys His Thr Gly 2690 2700

Glu Lys Pro Pro Gly Tyr Arg Thr Leu Gly Leu Val Thr Leu Gln 2705 2710

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Tyr Ala Tyr Arg Ser Ala Asp Val Phe Met Pro Tyr Ile Lys Ser Asn

Phe Asn Pro Val Thr Asp Ser Ala Leu Asn Val Ser Leu Thr Tyr Met

Tyr Gln Asp Gln Tyr Gly Lys Lys His Lys Lys Thr Ser Glu Asp Arg

Phe Lys Thr Asn Arg Asp Arg Ile Glu Leu Tyr Leu Lys Gly Tyr Thr

Leu Asn Arg Gly Ala Tyr Ser Phe Ser Pro Ser Ala Gly Phe Arg Tyr 100 105

Glu Ser Trp Asp Val Asn Tyr Asp Asn Pro Lys Lys Gln Asp Lys Trp 115 120 125

Lys Leu Glu Leu Arg Phe Tyr Pro Asn Met Thr Tyr Lys Leu Asn Asp 130 135 140

Gln Leu Ser Leu Tyr Met Asn Gly Phe Val Ala Pro Val Phe Phe Lys 145 150 155 160

Thr Gln Gln Glu Ser Arg Lys Asp Asn Asn Tyr Val Lys Gly Lys Leu 165 170 175

Gly Ala Lys Arg Tyr Asn Asn Asp Tyr Tyr Gln Glu Leu Gln Ile Leu 180 185 190

Gly Val Arg Tyr Lys Phe Asn Asn Asp Asn Thr Leu Trp Ala Ser Val

Tyr Asn Glu Arg Lys Tyr Asn Gln His Ser Ser Lys Tyr Asp Arg Trp 210 215 220

Gln Leu Arg Gly Gly Tyr Asp Phe Lys Val Thr Glu Glu Phe Val Leu 225 230 235 240

Ser Pro Phe Ile Arg Tyr Asp Leu Ser Tyr Arg Glu Lys Asn Leu Glu 245 250 255

Ser Thr Ser Asn Asn Gly Leu Ser Lys Asn Asn Lys Glu Ile Arg Thr 260 265 270

Gly Ala Ser Phe Ser Tyr Lys Ile Ile Pro Ser Val Lys Leu Val Gly
275 280 285

Glu Ile Tyr Arg Gln Thr Thr Asn Ile Glu Asn Tyr Tyr Gly Glu His
290 295 300

Ser Glu Asp Lys Asn Arg Met Phe Tyr Lys Leu Gly Ile Asn Lys Thr 305 310 315 320

Phe

(---

(;

<210> 45

<	2	1	1>	5	8	7
	_	_	_			

<212> PRT

<213> Escherichia coli

<400> 45

Met Gln His Arg Gln Lys Asn Ile Leu Thr Lys Thr Ser Leu Leu Ser 1 5 10 15

Arg Ala Leu Ser Val Pro Cys Cys Asp Met Phe Arg Arg Gly Ser Pro 20 25 30

Trp Ile Cys Tyr Leu Ser Leu Ser Val Phe Ser Gly Cys Phe Ile Pro 35 40 45

Ala Phe Ser Ser Pro Ala Ala Met Leu Ser Pro Gly Asp Arg Ser Ala 50 55 60

Ile Gln Gln Gln Gln Gln Leu Leu Asp Glu Asn Gln Arg Gln Arg 65 70 75 80

Asp Ala Leu Glu Arg Pro Leu Thr Ile Thr Pro Ser Pro Glu Thr Ser 85 90 95

Ala Gly Thr Glu Gly Pro Cys Phe Thr Val Ser Ser Ile Val Val Ser

Gly Ala Thr Arg Leu Thr Ser Ala Glu Thr Asp Arg Leu Val Pro Trp 115 120 125

Val Asn Gln Cys Leu Asn Ile Thr Gly Leu Thr Ala Val Thr Asp Ala 130 135 140

Val Thr Asp Gly Tyr Ile Arg Arg Gly Tyr Ile Thr Ser Arg Ala Phe 145 150 155 160

Leu Thr Glu Gln Asp Leu Ser Gly Gly Val Leu His Ile Thr Val Met
165 170 175

Glu Gly Arg Leu Gln Gln Ile Arg Ala Glu Gly Ala Asp Leu Pro Ala 180 185 190

Arg Thr Leu Lys Met Val Phe Pro Gly Met Glu Gly Lys Val Leu Asn 195 200 205

- Leu Arg Asp Ile Glu Gln Gly Met Glu Gln Ile Asn Arg Leu Arg Thr 210 215 220
- Glu Pro Val Gln Ile Glu Ile Ser Pro Gly Asp Arg Glu Gly Trp Ser 225 230 235 240
- Val Val Thr Leu Thr Ala Leu Pro Glu Trp Pro Val Thr Gly Ser Val 245 250 255
- Gly Ile Asp Asn Ser Gly Gln Lys Ser Thr Gly Thr Gly Gln Leu Asn 260 265 270
- Gly Val Leu Ser Phe Asn Asn Pro Leu Gly Leu Ala Asp Asn Trp Phe 275 280 285
- Val Ser Gly Gly Arg Ser Ser Asp Phe Ser Val Ser His Asp Ala Arg 290 295 300
- Asn Phe Ala Ala Gly Val Ser Leu Pro Tyr Gly Tyr Thr Leu Val Asp 305 310 315 320
- Tyr Thr Tyr Ser Trp Ser Asp Tyr Leu Ser Thr Ile Asp Asn Arg Gly 325 330 335
- Trp Arg Trp Arg Ser Thr Gly Asp Leu Gln Thr His Arg Leu Gly Leu
 340 345 350
- Ser His Val Leu Phe Arg Asn Gly Asp Met Lys Thr Ala Leu Thr Gly 355 360 365
- Gly Leu Gln His Arg Ile Ile His Asn Tyr Leu Asp Asp Val Leu Leu 370 375 380
- Gln Gly Ser Ser Arg Lys Leu Thr Ser Phe Ser Val Gly Leu Asn His 385 390 395 400
- Thr His Lys Phe Leu Gly Gly Val Gly Thr Leu Asn Pro Val Phe Thr 405 410 415
- Arg Gly Met Pro Trp Phe Gly Ala Glu Ser Asp His Gly Lys Arg Gly 420 425 430
- Asp Leu Pro Val Asn Gln Phe Arg Lys Trp Ser Val Ser Ala Ser Phe

435 440 445

Gln Arg Pro Val Thr Asp Arg Val Trp Trp Leu Thr Ser Ala Tyr Ala 450 455 460

Gln Trp Ser Pro Asp Arg Leu His Gly Val Glu Gln Leu Ser Leu Gly 465 470 475 480

Gly Glu Ser Ser Val Arg Gly Phe Lys Asp Gln Tyr Ile Ser Gly Asn 485. 490 495

Asn Gly Gly Tyr Leu Arg Asn Glu Leu Ser Trp Ser Leu Phe Ser Leu 500 505 510

Pro Tyr Val Gly Thr Val Arg Ala Val Ala Ala Leu Asp Gly Gly Trp 515 520 525

Leu His Ser Asp Ser Asp Pro Tyr Ser Ser Gly Thr Leu Trp Gly 530 540

Ala Ala Ala Gly Leu Ser Thr Thr Ser Gly His Val Ser Gly Ser Phe 545 550 555 560

Thr Ala Gly Leu Pro Leu Val Tyr Pro Asp Trp Leu Ala Pro Asp His
565 570 575

Leu Thr Val Tyr Trp Arg Val Ala Val Ala Phe 580 585

<210> 46

<211> 744

<212> PRT

<213> Escherichia coli

<400> 46

Met Asn Lys His Thr Leu Leu Leu Thr Val Leu Phe Leu Asn Leu Ile

1 10 15

Cys Thr Pro Val Phe Ala Gln Asn Trp Gln Val Ala Thr Phe Gly Gln 20 25 30

Ser Thr Asp Leu Asn Phe Ser Ser Leu Ile Asp Ser Ala Lys Ile Gly 35 40 45

- Arg Asn Asn Ala Trp Leu Ala Gly Asn Asn Asn Phe Leu Glu Ala Gly 50 55 60
- Lys Phe Tyr Thr Leu Pro Thr Asp Phe Phe Ile Glu Ser Arg Gly Gly 65 70 75 80
- Lys Ile Ala Asn Ser His Asp Gly Met Thr Val Phe Tyr Thr Ile Val 85 90 95
- Pro Val Thr Gln Thr Phe Arg Leu Glu Ala Asp Leu Thr Leu Glu Gln
 100 105 110
- Ile Gly Pro Glu Val Asn Gly Lys Ser Pro Ala Gly Gln Glu Gly Ala 115 120 125
- Gly Leu Phe Val Arg Asp Ile Ile Gly Pro Gln Arg Gln Glu Pro Gln 130 140
- Ala Phe Ile Thr Gln Asn Lys Lys Asn Asp Asn Leu Val Gln Ile Thr 165 170 175
- Ser Ile Val Arg Glu Gly Val Ile Lys Thr Trp Gly Asn Glu Gly Ile 180 185 190
- Thr Ile Lys Lys Gln Pro Ile Ile Glu Asn Ile Asn Phe Thr Gln Lys 195 200 205
- Arg Asn Ile His Met Thr Ile Glu Arg Leu Pro Glu Lys Phe Ile Leu 210 215 220
- Thr Ala Phe Asp Thr Asp Arg Lys Glu Asn Gln Ser Trp Gln Phe Ser 225 230 235 240
- Asp Tyr Ser Gly Phe Met Asn Gln Leu Asp Asn Asn Ser Leu Ala Ile 245 250 255
- Gly Phe Phe Ala Ala Arg Asn Ala Lys Leu Arg Val Lys Asn Ala Ser 260 265 270
- Phe Lys Pro Gly Lys Pro Leu Val Asp Tyr Lys Gln Leu Thr Ser Arg

(::

117

		275					280					285			
Gln	Phe 290	Ser	Arg	Val	Arg	His 295	Lys	Ala	Pro	Glu	Leu 300	Phe	Leu	Ala	Ser
Pro 305	Gln	Ser	Val	Val	Arg 310	Asn	Ser	Thr	Thr	Leu 315	Gln	Phe	Leu	Ala	Asn 320
Gln	Ala	Gly	Ile	Val 325	Ser	Ile	Asp	Asn	Asp 330	Lys	Gln	Thr	Lys	Gln 335	Val
Gln	Ala	Gly	Glu 340	Leu	Val	Gln	Phe	Pro 345	Val	Thr	Leu	Gln	Lys 350	Lys	His
Asn	Asp	Phe 355	Thr	Val	Asn	Phe	Asn 360	Val	Asp	Gly	Asn	Ile 365	Ser	Lys	Lys
Ala	Ile 370	Arg	Ile	Glu	Gln	Val 375	Lys	Ser	Asn	Leu	Thr 380	Asp	Pro	Tyr	Glu
Ile 385	Tyr	Val	Cys	Ser	Asp 390	Cys	Arg	Gln	Gly	Ala 395	Arg	Gly	Ser	Lys	Asn 400
Asp	Pro	Val	Asp	Leu 405	Gln	Thr	Ala	Val	Lys 410	Phe	Val	Ala	Pro	Gly 415	Gly
Asn	Ile	Tyr	Leu 420	Asn	Asp	Gly	Gln	Tyr 425	His	Gly	Ile	Thr	Leu 430	Asp	Arg
Glu	Leu	Ser 435	Gly	Ile	Pro	Gly	Lys 440	Tyr	Lys	Thr	Ile	Ser 445	Ala	Ile	Asn
Pro	His 450	Lys	Ala	Ile	Phe	Ile 455	Asn	Dys	Thr	Phe	Asn 460	Leu	Asp	Ala	Ser
Tyr 465	Trp	His	Leu	Lys	Ser 470	Val	Val	Phe	Asp	Gly 475	Asn	Val	Asp	Asn	Gly 480
Asn	Asn	Lys	Pro	Ala 485	Tyr	Leu	Arg	Ile	Ala 490	Gly	Ser	Tyr	Asn	Ile 495	Ile
Glu	His	Val	Ile 500	Ala	Arg	Asn	Asn	Asp 505	Asp	Thr	Gly	Ile	Ser 510	Ile	Ser

Ala	Lys	Asp 515	Lys	Asn	Arg	Phe	Phe 520	Trp	Pro	Ala	His	Asn 525	Leu	Val	Leu

Asn Ser Asp Ser Tyr Asn Asn Leu Asp Leu Ser Gly Ile Asn Ala Asp 530 540

Gly Phe Ala Ala Lys Leu Gly Val Gly Pro Gly Asn Ile Phe Arg Gly 545 550 555 560

Cys Ile Ala His Asn Asn Ala Asp Asp Gly Trp Asp Leu Phe Asn Lys 565 570 575

Ile Glu Asp Gly Pro Asn Ala Ser Val Thr Ile Glu Asn Ser Val Ala 580 585 590

Tyr Glu Asn Gly Leu Pro Tyr Asn Lys Ala Asp Ile Leu Lys Gly Ser 595 600 605

Ile Gly Asn Gly Gly Glu Gly Gln Pro Ser Lys Ser Gln Val Ile Asn 610 615 620

Ser Ile Ala Ile Asn Asn Asn Met Asp Gly Phe Thr Asp Asn Phe Asn 625 630 635 640

Thr Gly Ser Leu Ile Val Arg Asn Asn Ile Ala Met Asn Asn Ala Arg 645 650 655

Tyr Asn Tyr Ile Leu Arg Thr Asn Pro Tyr Lys Phe Pro Ser Ser Ile 660 665 670

Leu Phe Asp Asn Asn Tyr Ser Ile Arg Asp Asp Trp Glu Asn Lys Ile 675 680 . 685

Lys Asp Phe Leu Gly Asp Thr Val Asn Ser Val Asn Tyr Lys Leu Leu 690 695 700

Val Ser His Glu Thr Gly Pro Val Gln Lys Asp Leu Phe Phe Thr Arg 705 710 715 720

Asp Asp Ser Gly Asn Ile Ile Tyr Pro Asp Phe Phe Leu Asn Ile Ile 725 730 735

(

119

Asn Lys Phe Asn Glx Thr Met Pro 740

<210> 47

<211> 136

<212> PRT

<213> Escherichia coli

<400> 47

Met Lys Thr Phe Ile Lys Thr Leu Leu Val Ala Val Thr Ile Leu Phe 1 5 10 15

Ser Val Phe Ala Thr Ala Lys Gln Val Lys Leu Pro Asn Asn Ile Lys 20 25 30

Tyr Val Asn Thr Thr Glu Ala Phe Ser Cys Thr Glu Ile Asp Gly Met 35 40 45

Asn Cys Gln Thr Lys Asn Pro Phe Asn Tyr Lys Asp Asn Ser Tyr Val 50 55 60

Phe Val Leu Glu Arg Gly Gly Ala Trp Cys Tyr Asp Tyr Thr Val Ser 65 70 75 80

Val Leu Asn Leu Lys Thr Gly Lys Ala Gln Met Leu Glu Tyr Lys Asp 85 90 95

Asn Gln Leu Cys Ser Gly Ser Asn Lys Pro Phe Phe Glu Ile Lys Asn 100 105 110

Gly Val Pro Thr Val Gly Val Ile Asp Thr Ser Gly Lys Pro Val Val 115 120 125

Val Ala Leu Asp Lys Leu Lys Thr : 130 135

<210> 48

<211> 225

<212> PRT

<213> Escherichia coli

<400> 48

Met Gln Leu Pro Val Lys Leu Leu Met Ser Leu Ile Ser Leu Val Ser I 10 15

Val Ile Ala Arg Ala Gly Lys Tyr Lys Asn Tyr Ile Arg Asp Glu Ile 20 25 30

Lys Tyr Trp Arg Tyr Thr Ser Tyr Lys Gly Glu Phe Pro Glu Gly 35 40 45

Phe Thr Asp Glu Lys Phe Ser Ser Ala Ile Tyr Asn Gly Arg Ile Phe 50 55 60

Thr Met Lys Arg Leu His Thr Leu Met Leu Phe Leu Ala Val Leu Phe 65 70 75 80

Thr Gly Phe Asn Val Glu Ala Ala Ser Val Lys Gln Ala Leu Ser Cys 85 90 · 95

Asp Pro Asn Ala Arg Ala Glu Gln Pro Gly Ala Cys Pro Thr Thr Tyr
100 105 110

Glu Leu Tyr Glu Gly Asp Ala Ala Tyr Lys Ala Ala Leu Asp Lys Ala 115 120 125

Leu Lys Pro Val Gly Leu Ser Gly Met Phe Gly Lys Gly Gly Tyr Met 130 135 140

Asp Gly Pro Gly Gly Asn Val Thr Pro Val Thr Ile Asn Gly Thr Val 145 150 155 160

Trp Leu Gln Gly Asp Gly Cys Lys Ala Asn Thr Cys Gly Trp Asp Phe 165 . 170 175

Ile Val Thr Leu Tyr Asn Pro Lys Thr His Glu Val Val Gly Tyr Arg
180 185 190

Tyr Phe Gly Leu Asp Asp Pro Ala Tyr Leu Val Trp Phe Gly Glu Ile 195 200 205

Gly Val His Glu Phe Ala Tyr Leu Val Lys Asn Tyr Val Ala Ala Val 210 215 220

Asn 225

<210> 49

<	2	Τ	1	>	7	2	1
	_	-	_		_	_	

<212> PRT

<213> Escherichia coli

<400> 49

Met Lys Thr Gln Ile Thr Phe Ala Ala Leu Leu Pro Ala Leu Ala Ser 1 5 10 15

Phe Ile Pro Leu His Ala His Ala Ser Ser Thr Ser Glu Asp Glu Met 20 25 30

Ile Val Thr Gly Asn Thr Ala Ala Asp Thr Thr Asp Ser Ala Ala Gly
35 40 45

Ala Gly Phe Lys Thr Asn Asp Ile Asp Val Gly Pro Leu Gly Thr Lys 50 55 60

Ser Trp Ile Glu Thr Pro Tyr Ser Ser Thr Thr Val Thr Lys Glu Met 70 75 80

Ile Glu Asn Gln Gln Ala Gln Ser Val Ser Glu Met Leu Lys Tyr Ser 85 90 95

Pro Ser Thr Gln Met Gln Ala Arg Gly Gly Met Asp Val Gly Arg Pro 100 105 110

Gln Ser Arg Gly Met Gln Gly Ser Val Val Ala Asn Ser Arg Leu Asp 115 120 125

Gly Leu Asn Ile Val Ser Thr Thr Ala Phe Pro Val Glu Met Leu Glu 130 135 140

Arg Met Asp Val Leu Asn Ser Leu Thr Gly Ala Leu Tyr Gly Pro Ala 145 150 155 160

Ser Pro Ala Gly Gln Phe Asn Phe Val Ala Lys Arg Pro Thr Glu Glu 165 170 175

Thr Leu Arg Lys Val Thr Leu Gly Tyr Gln Ser Arg Ser Ala Phe Thr 180 185 190

Gly His Ala Asp Leu Gly Gly His Phe Asp Glu Asn Lys Arg Phe Gly 195 200 205

0207455340 1

Tyr	Arg	Val	Asn	Leu	Leu	Asp	Gln	Glu	Gly	Glu	Gly	Asn	Val	Asp	Asp
	210					215					220				

Ser Thr Leu Arg Arg Lys Leu Val Ser Val Ala Leu Asp Trp Asn Ile 225 230 235 240

Gln Pro Gly Thr Gln Leu Gln Leu Asp Ala Ser His Tyr Glu Phe Ile 245 250 255

Gln Lys Gly Tyr Val Gly Ser Phe Asn Tyr Gly Pro Asn Val Lys Leu
260 265 270

Pro Ser Ala Pro Asn Pro Lys Asp Lys Asn Leu Ala Leu Ser Thr Ala 275 280 285

Gly Asn Asp Leu Thr Thr Asp Thr Ile Ser Thr Arg Leu Ile His Tyr 290 295 300

Phe Asn Asp Asp Trp Ser Met Asn Ala Gly Val Gly Trp Gln Gln Ala 305 310 315 320

Asp Arg Ala Met Arg Ser Val Ser Ser Lys Ile Leu Asn Asn Gln Gly 325 330 335

Asp Ile Ser Arg Ser Met Lys Asp Ser Thr Ala Ala Gly Arg Phe Arg 340 345 350

Val Leu Ser Asn Thr Ala Gly Leu Asn Gly His Ile Asp Thr Gly Ser 355 360 365

Ile Gly His Asp Leu Ser Leu Ser Thr Thr Gly Tyr Val Trp Ser Leu 370 380

Tyr Ser Ala Lys Gly Thr Gly Ser Ser Tyr Ser Trp Gly Thr Thr Asn 385 390 395 400

Met Tyr His Pro Asp Ala Ile Asp Glu Gln Gly Asp Gly Lys Ile Arg 405 410 415

Thr Gly Gly Pro Arg Tyr Arg Ser Ser Val Asn Thr Gln Gln Ser Val 420 425 430

Thr Leu Gly Asp Thr Val Thr Phe Thr Pro Gln Trp Ser Ala Met Phe

125	440	445

		435					440					445			
Tyr	Leu 450	Ser	Gln	Ser	Trp	Leu 455	Gln	Thr	Lys	Asn	Tyr 460	Asp	Lys	His	Gly
Asn 465	Gln	Thr	Asn	Gln	Val 470	Asp	Glu	Asn	Gly	Leu 475	Ser	Pro	Asn	Ala	Ala 480
Leu	Met	Tyr	Lys	Ile 485	Thr	Pro	Asn	Thr	Met 490	Ala	Tyr	Val	Ser	Tyr 495	Ala
Asp	Ser	Leu	Glu 500	Gln	Gly	Gly	Thr	Ala 505	Pro	Thr	Asp	Glu	Ser 510	Val	Lys
Asn	Ala	Gly 515	Gln	Thr	Leu	Asn	Pro 520	Tyr	Arg	Ser	Lys	Gln 525	Tyr	Glu	Val
Gly	Leu 530	Lys	Ser	Asp	Ile	Gly 535	Glu	Met	Asn	Leu	Gly 540	Ala	Ala	Leu	Phe
Arg 545	Leu	Glu	Arg	Pro	Phe 550	Ala	Tyr	Leu	Asp	Thr 555	Asp	Asn	Val	Tyr	Lys 560
Glu	Gln	Gly	Asn	Gln 565	Val	Asn	Asn	Gly	Leu 570	Glu	Leu	Thr	Ala	Ala 575	Gly
Asn	Val	Trp	Gln 580	Gly	Leu	Asn	Ile	Tyr 585	Ser	Gly	Val	Thr	Phe 590	Leu	Asp
Pro	Lys	Leu 595	Lys	Asp	Thr	Ala	Asn 600	Ala	Ser	Thr	Ser	Asn 605	Lys	Gln	Val
Val	Gly 610	Val	Pro	Lys	Val	Gln 615	Ala	Asn	Leu	Leu	Ala 620	Glu	Tyr	Ser	Leu
Pro 625	Ser	Ile	Pro	Glu	Trp 630	Val	Tyr	Ser	Ala	Asn 635	Val	His	Tyr	Thr	Gly 640
Lys	Arg	Ala	Ala	Asn 645	Asp	Thr	Asn	Thr	Ser 650	Tyr	Ala	Ser	Ser	Tyr 655	Thr
Thr	Trp	Asp	Leu 660	Gly	Thr	Arg	Tyr	Thr 665	Thr	Lys	Val	Ser	Asn 670	Val	Pro

Thr Thr Phe Arg Val Val Val Asn Asn Val Phe Asp Lys His Tyr Trp 675 680

Ala Ser Ile Phe Pro Ser Gly Thr Asp Gly Asp Asn Gly Ser Pro Ser 695

Ala Phe Ile Gly Gly Gly Arg Glu Val Arg Ala Ser Val Thr Phe Asp 715

Phe

<210> 50 <211> 669 <212> PRT <213> Escherichia coli <400> 50

Met Lys Asn Ile Thr Leu Trp Gln Arg Leu Arg Gln Val Ser Ile Ser

Thr Ser Leu Arg Cys Ala Phe Leu Met Gly Ala Leu Leu Thr Leu Ile

Val Ser Ser Val Ser Leu Tyr Ser Trp His Glu Gln Ser Ser Gln Ile

Arg Tyr Ser Leu Asp Lys Tyr Phe Pro Arg Ile His Ser Ala Phe Leu 50

Ile Glu Gly Asn Leu Asn Leu Val Val Asp Gln Leu Asn Glu Phe Leu

Gln Ala Pro Asn Thr Thr Val Arg Leu Gln Leu Arg Thr Gln Ile Ile

Gln His Leu Asp Thr Ile Glu Arg Leu Ser Arg Gly Leu Ser Ser Arg 100 105

Glu Arg Gln Gln Leu Thr Val Ile Leu Gln Asp Ser Arg Ser Leu Leu 115 120

Ser Glu Leu Asp Arg Ala Leu Tyr Asn Met Phe Leu Leu Arg Glu Lys

125

	130					135					140				
Val 145	Ser	Glu	Leu	Ser	Ala 150	Arg	Ile	Asp	Trp	Leu 155	His	Asp	Asp	Phe	Thr 160
Thr	Glu	Leu	Asn	Ser 165	Leu	Val	Gln	Asp	Phe 170	Thr	Trp	Gln	Gln	Gly 175	Thr
Leu	Leu	Asp	Gln 180	Ile	Ala	Ser	Arg	Gln 185	Gly	Asp	Thr	Ala	Gln 190	Tyr	Leu
Lys	Arg	Ser 195	Arg	Glu	Val	Gln	Asn 200	Glu	Gln	Gln	Gln	Val 205	Tyr	Thr	Let
Ala	Arg 210	Ile	Glu	Asn	Gln	Ile 215	Val	Asp	Asp	Leu	Arg 220	Asp	Arg	Leu	Asn
Glu 225	Leu	Lys	Ser	Gly	Arg 230	Asp	Asp	Asp	Ile	Gln 235	Val	Glu	Thr	His	Leu 240
Arg	Tyr	Phe	Glu	Asn 245	Leu	Lys	Lys	Thr	Ala 250	Asp	Glu	Asn	Ile	Arg 255	Met
Leu •	Asp	Asp	Trp 260	Pro	Gly	Thr	Ile	Thr 265	Leu	Arg	Gln	Thr	Ile 270	Asp	Glu
Leu	Leu	Asp 275	Met	Gly	Ile	Val	Lys 280	Asn	Lys	Met	Pro	Asp 285	Thr	Met	Arg
Glu	Tyr 290	Val	Ala	Ala	Gln	Lys 295	Ala	Leu	Glu	Asp	Ala 300	Ser	Arg	Thr	Arg
Glu 305	Ala	Thr	Gln	Gly	Arg 310	Phe	Arg	Thr	Leu	Leu 315	Glu	Ala	Gln	Leu	Gly 320
Ser	Thr	His	Gln	Gln 325	Met	Gln	Met	Phe	Asn 330	Gln	Arg	Met	Glu	Gln 335	Ile
Val	His	Val	Ser 340	Gly	Gly	Leu	Ile	Leu 345	Val	Ala	Thr	Ala	Leu 350	Ala	Let
Leu	Leu	Ala 355	Trp	Val	Phe	Asn	His 360	Tyr	Phe	Ile	Arg	Ser 365	Arg	Leu	Val

Lys Arg Phe Thr Leu Leu Asn Gln Ala Val Val Gln Ile Gly Leu Gly 370 375 380

Gly Thr Glu Thr Thr Ile Pro Val Tyr Gly Asn Asp Glu Leu Gly Arg 385 390 395 400

Ile Ala Gly Leu Leu Arg His Thr Leu Gly Gln Leu Asn Val Gln Lys
405
410
415

Gln Gln Leu Glu Gln Glu Ile Thr Asp Arg Lys Val Ile Glu Ala Asp
420 425 430

Leu Arg Ala Thr Gln Asp Glu Leu Ile Gln Thr Ala Lys Leu Ala Val 435 440 445

Val Gly Gln Thr Met Thr Thr Leu Ala His Glu Ile Asn Gln Pro Leu 450 455 460

Asn Ala Leu Ser Met Tyr Leu Phe Thr Ala Arg Arg Ala Ile Glu Gln 465 470 475 480

Thr Gln Lys Glu Gln Ala Ser Met Met Leu Gly Lys Ala Glu Gly Val 485 490 495

Ile Ser Arg Ile Asp Ala Ile Ile Arg Ser Leu Arg Gln Phe Thr Arg 500 505 510

Arg Ala Glu Leu Glu Thr Ser Leu His Ala Val Asp Leu Ala Gln Met 515 520 525

Phe Ser Ala Ala Trp Glu Leu Leu Ala Met Arg His Arg Ser Leu Gln 530 535 , 540

Ala Thr Leu Val Leu Pro Gln Gly Thr Ala Thr Val Ser Gly Asp Glu 545 550 555 560

Val Arg Thr Gln Gln Val Leu Val Asn Val Leu Ala Asn Ala Leu Asp
565 570 575

Val Cys Gly Gln Gly Ala Val Ile Thr Val Asn Trp Gln Met Gln Gly 580 585 590

(: :

- Lys Thr Leu Asn Val Phe Ile Gly Asp Asn Gly Pro Gly Trp Pro Glu 600
- Ala Leu Leu Pro Ser Leu Leu Lys Pro Phe Thr Thr Ser Lys Glu Val 610
- Gly Leu Gly Ile Gly Leu Ser Ile Cys Val Ser Leu Met Glu Gln Met 630
- Lys Gly Glu Leu Arg Leu Ala Ser Thr Met Thr Arg Asn Ala Cys Val 650
- Val Leu Gln Phe Arg Leu Thr Asp Val Glu Asp Ala Lys
- <210> 51

- <211> 753 <212> PRT <213> Escherichia coli <400> 51
- Met Asn Val Ile Lys Leu Ala Ile Gly Ser Gly Ile Leu Leu Ser
- Cys Gly Ala Tyr Ser Gln Ser Ile Ser Glu Lys Thr Asn Ser Asp Lys 20
- Lys Gly Ala Ala Glu Phe Ser Pro Leu Ser Val Ser Val Gly Lys Thr 35
- Thr Ser Glu Glu Glu Ala Leu Glu Lys Thr Gly Ala Thr Ser Ser Arg
- Thr Thr Asp Lys Asn Leu Gln Ser Leu Asp Ala Thr Val Arg Ser Met
- Pro Gly Thr Tyr Thr Gln Ile Asp Pro Gly Gln Gly Ala Ile Ser Val
- Asn Ile Arg Gly Met Ser Gly Phe Gly Arg Val Asn Thr Met Val Asp 100 110
- Gly Ile Thr Gln Ser Phe Tyr Gly Thr Ser Thr Ser Gly Thr Thr 115 120 125

- His Gly Ser Thr Asn Asn Met Ala Gly Val Leu Ile Asp Pro Asn Leu 130 135 140
- Leu Val Ala Val Asp Val Thr Arg Gly Asp Ser Ser Gly Ser Glu Gly 145 150 155 160
- Ile Asn Ala Leu Ala Gly Ser Ala Asn Met Arg Thr Ile Gly Val Asp 165 170 175
- Asp Val Ile Phe Asn Gly Asn Thr Tyr Gly Leu Arg Ser Arg Phe Ser 180 185 190
- Val Gly Ser Asn Gly Leu Gly Arg Ser Gly Met Ile Ala Leu Gly Gly 195 200 205
- Lys Ser Asp Ala Phe Thr Asp Thr Gly Ser Ile Gly Val Met Ala Ala 210 215 220
- Val Ser Gly Ser Ser Val Tyr Ser Asn Phe Ser Asn Gly Ser Gly Ile 225 230 235 240
- Asn Ser Lys Glu Phe Gly Tyr Asp Lys Tyr Met Lys Gln Asn Pro Lys 245 250 255
- Ser Gln Leu Tyr Lys Met Asp Ile Arg Pro Asp Glu Phe Asn Ser Phe 260 265 270
- Glu Leu Ser Ala Arg Thr Tyr Glu Asn Lys Phe Thr Arg Arg Asp Ile 275 280 285
- Thr Ser Asp Asp Tyr Tyr Ile Lys Tyr His Tyr Thr Pro Phe Ser Glu 290 295 300
- Leu Ile Asp Phe Asn Val Thr Ala Ser Thr Ser Arg Gly Asn Gln Lys 305 310 315 320
- Tyr Arg Asp Gly Ser Leu Tyr Thr Phe Tyr Lys Thr Ser Ala Gln Asn 325 330 335
- Arg Ser Asp Ala Leu Asp Ile Asn Asn Thr Ser Arg Phe Thr Val Ala 340 345 350

Asp	Asn	Asp 355	Leu	Glu	Phe	Met	Leu 360		Ser	Lys	Leu	Met 365		Thr	Arg
Tyr	Asp 370	Arg	Thr	Ile	His	Ser 375	Ala	Ala	Gly	Asp	Pro 380		Ala	Asn	Glr
Glu 385	Ser	Ile	Glu	Asn	Asn 390	Pro	Phe	Ala	Pro	Ser 395	Gly	Gln	Gln	Asp	Ile 400
Ser	Ala	Leu	Tyr	Thr 405	Gly	Leu	Lys	Val	Thr 410	Arg	Gly	Ile	Trp	Glu 415	Ala
Asp	Phe	Asn	Leu 420	Asn	Tyr	Thr	Arg	Asn 425	Arg	Ile	Thr	Gly	Tyr 430	Lys	Pro
Ala	Cys	Asp 435	Ser	Arg	Val	Ile	Cys 440	Val	Pro	Gln	Gly	Ser 445	Tyr	Asp	Ile
Asp	Asp 450	Lys	Glu	Gly	Gly	Phe 455	Asn	Pro	Ser	Val	Gln 460	Leu	Ser	Ala	Gln
Val 465	Thr	Pro	Trp	Leu	Gln 470	Pro	Phe	Ile	Gly	Tyr 475	Ser	Lys	Ser	Met	Arg 480
Ala	Pro	Asn	Ile	Gln 485	Glu	Met	Phe	Phe	Ser 490	Asn	Ser	Gly	Gly	Ala 495	Ser
Met	Asn	Pro	Phe 500	Leu	Lys	Pro	Glu	Arg 505	Ala	Glu	Thr	Trp	Gln 510	Ala	Gly
Phe	Asn	Ile 515	Asp	Thr	Arg	Asp	Leu 520	Leu !	Val	Glu	Gln	Asp 525	Ala	Leu	Arg
Phe	Lys 530	Ala	Leu	Ala	Tyr	Arg 535	Ser	Arg	Ile	Gln	Asn 540	Tyr	Ile	Tyr	Ser
31u 545	Ser	Tyr	Leu	Val	Cys 550	Ser	Gly	Gly	Arg	Lys 555	Cys	Ser	Leu	Pro	Glu 560
/al	Ile	Gly	Asn	Gly 565	Trp	Glu	Gly	Ile	Ser 570	Asp	Glu	Tyr	Ser	Asp 575	Asn

. . . .

130

Met Tyr Ile Tyr Val Asn Ser Ala Ser Asp Val Ile Ala Lys Gly Phe 580 585 590

Glu Leu Glu Met Asp Tyr Asp Ala Gly Phe Ala Phe Gly Arg Leu Ser $595 \hspace{1.5cm} 600 \hspace{1.5cm} 605$

Phe Ser Gln Gln Gln Thr Asp Gln Pro Thr Ser Ile Ala Ser Thr His 610 620

Phe Gly Ala Gly Asp Ile Thr Glu Leu Pro Arg Lys Tyr Met Thr Leu 625 630 635 640

Asp Thr Gly Val Arg Phe Phe Asp Asn Ala Leu Thr Leu Gly Thr Ile 645 650 655

Ile Lys Tyr Thr Gly Lys Ala Arg Arg Leu Ser Pro Asp Phe Glu Gln 660 665 670

Asp Glu His Thr Gly Ala Ile Ile Lys Gln Asp Leu Pro Gln Ile Pro 675 680 685

Thr Ile Ile Asp Leu Tyr Gly Thr Tyr Glu Tyr Asn Arg Asn Leu Thr 690 695 700

Leu Lys Leu Ser Val Gln Asn Leu Met Asn Arg Asp Tyr Ser Glu Ala 705 710 715 720

Leu Asn Lys Leu Asn Met Met Pro Gly Leu Gly Asp Glu Thr His Pro 725 730 735

Ala Asn Ser Ala Arg Gly Arg Thr Trp Ile Phe Gly Gly Asp Ile Arg
740 745 750

•

Phe

<210> 52

<211> 133

<212> PRT

<213> Escherichia coli

<400> 52

Met Ser Ser Lys Thr Lys Cys Trp Leu Trp Met Leu Leu Val Ile Leu 1 5 10 15

Ser Glu Thr Ser Ala Thr Ser Thr Leu Lys Met Phe Asp Asn Ser Glu

Gly Met Thr Lys Thr Leu Leu Leu Ala Leu Ile Val Val Leu Tyr Cys

Ile Cys Tyr Tyr Ser Leu Ser Arg Ala Val Lys Asp Ile Pro Val Gly 50

Leu Ala Tyr Ala Thr Trp Ser Gly Thr Gly Ile Leu Met Val Ser Thr 70 75

Leu Gly Ile Leu Phe Tyr Gly Gln His Pro Asp Thr Ala Ala Ile Ile 90

Gly Met Val Ile Ile Ala Ser Gly Ile Ile Ile Met Asn Leu Phe Ser 105

Lys Met Gly Ser Glu Glu Ala Glu Glu Thr Pro Val Thr Asn Leu Asp 115

Lys Lys Ile Ala Asn 130

<210> 53 <211> 286

<212> PRT

<213> Escherichia coli

<400> 53

Met Tyr Ile Lys Lys His Trp Ile Ala Leu Ser Ile Leu Leu Ile Pro 5

Cys Ile Gly Asn Ala Gln Glu Ile Lys Ile Asp Glu Ser Trp Leu His

Gln Ser Leu Asn Val Ile Gly Arg Thr Asp Ser Arg Phe Gly Pro Arg

Leu Thr Asn Asp Leu Tyr Pro Glu Tyr Thr Val Ala Gly Arg Lys Asp

Trp Phe Asp Phe Tyr Gly Tyr Val Asp Leu Pro Lys Phe Phe Gly Val 70

Gly	Ser	His	Tyr	Asp	Val	${ t Gly}$	Ile	Trp	Asp	Glu	Gly	Ser	Pro	Leu	Phe
				85					90					95	

Thr Glu Ile Glu Pro Arg Phe Ser Ile Asp Lys Leu Thr Gly Leu Asn 100 105

Leu Ala Phe Gly Pro Phe Lys Glu Trp Phe Ile Ala Asn Asn Tyr Val 120

Tyr Asp Met Gly Asp Asn Gln Ser Ser Arg Gln Ser Thr Trp Tyr Met

Gly Leu Gly Thr Asp Ile Asp Thr Gly Leu Pro Ile Lys Leu Ser Ala 150

Asn Ile Tyr Ala Lys Tyr Gln Trp Gln Asn Tyr Gly Ala Ala Asn Glu

Asn Glu Trp Asp Gly Tyr Arg Phe Lys Ile Lys Tyr Ser Ile Pro Leu

Thr Asn Leu Phe Gly Gly Arg Leu Val Tyr Asn Ser Phe Thr Asn Phe

Asp Phe Gly Ser Asp Leu Ala Asp Lys Ser His Asn Asn Lys Arg Thr

Ser Asn Ala Ile Ala Ser Ser His Ile Leu Ser Leu Leu Tyr Glu His

Trp Lys Phe Ala Phe Thr Leu Arg Tyr Phe His Asn Gly Gly Gln Trp 250

Asn Ala Gly Glu Lys Val Asn Phe Gly Asp Gly Pro Phe Glu Leu Lys

Asn Thr Gly Trp Gly Thr Tyr Thr Thr Ile Gly Tyr Gln Phe

<210> 54

<211> 172 <212> PRT

<213> Escherichia coli <400> 54

Met Arg Ile Ala Pro Arg Thr Phe Phe Ala Ile Ser Ala Leu Ala Phe 1 5 10 15

Ile Val Ala Ser Gly Phe Ser Phe Trp Arg Leu Ser Pro Ala Glu Asn 20 25 30

Thr Gly Ile Met Ser Cys Ser Thr Lys Gly Ile Met Arg Phe Glu Asn 35 40 45

Met Glu Lys Glu Asn Val Asn Gly Asn Ile His Phe Asn Phe Gly Ser 50 55 60

Gln Gly Lys Gly Ser Met Val Leu Glu Gly Tyr Thr Asp Ser Ala Ala 65 70 75 80

Gly Trp Leu Tyr Leu Gln Arg Tyr Val Lys Phe Thr Tyr Thr Ser Lys
85 90 95

Arg Val Ser Ala Thr Glu Arg His Tyr Arg Ile Ser Gln Trp Glu Ser 100 105 110

Ser Ala Ser Ser Ile Asp Glu Ser Pro Asp Val Ile Phe Asp Tyr Phe 115 120 125

Met Arg Glu Met Ser Asp Ser His Asp Gly Leu Phe Leu Asn Ala Gln 130 135 140

Lys Leu Asn Asp Lys Ala Ile Leu Leu Ser Ser Ile Asn Ser Pro Leu 145 150 155 160

Trp Ile Cys Thr Leu Lys Ser Gly Ser Lys Leu Asp 165 170

<210> 55

<211> 182

<212> PRT

<213> Escherichia coli

<400> 55

BNSDOCID: >WO

Met Lys Ile Lys Val Ile Ala Leu Ala Thr Phe Val Ser Ala Val Phe 1 5 10 15

Ala Gly Ser Ala Met Ala Tyr Asp Gly Thr Ile Thr Phe Thr Gly Lys
20 25 30

Val Val Ala Gln Thr Cys Thr Val Asn Thr Ser Asp Lys Asp Leu Ala 35 40 45

Val Thr Leu Pro Thr Val Ala Thr Ser Ser Leu Lys Asp Asn Ala Ala 50 55 60

Thr Ser Gly Leu Thr Pro Phe Ala Ile Arg Leu Thr Gly Cys Ala Thr 65 70 75 80

Gly Met Asn Ser Ala Gln Asn Val Lys Ala Tyr Phe Glu Pro Ser Ser 85 90 95

Asn Ile Asp Leu Ala Thr His Asn Leu Lys Asn Thr Ala Thr Pro Thr 100 105 110

Lys Ala Asp Asn Val Gln Ile Gln Leu Leu Asn Ser Asn Gly Thr Ser 115 120 125

Thr Ile Leu Leu Gly Glu Ala Asp Asn Gly Gln Asp Val Gln Ser Glu 130 135 140

Thr Ile Gly Ser Asp Gly Ser Ala Thr Leu Arg Tyr Met Ala Gln Tyr 145 150 155 160

Tyr Ala Thr Gly Gln Ser Thr Ala Gly Asp Val Lys Ala Thr Val His 165 170 175

Tyr Thr Ile Ala Tyr Glu 180

<210> 56

<211> 359

<212> PRT

<213> Escherichia coli

<400> 56

Met Lys Arg Ile Phe Phe Ile Pro Leu Phe Leu Ile Leu Leu Pro Lys 1 5 10 15

Leu Ala Val Ala Gly Pro Asp Asp Tyr Val Pro Ser Gln Ile Ala Val 20 25 30

Asn	Thr	Ser	Thr	Leu	Pro	Gly	Val	Val	Ile	Gly	Pro	Ala	Asp	Ala	His
		35					40					45			

- Thr Tyr Pro Arg Val Ile Gly Glu Leu Ala Gly Thr Ser Asn Gln Tyr 50 55
- Val Phe Asn Gly Gly Ala Ile Ala Leu Met Arg Gly Lys Phe Thr Pro 65 70 75 80
- Ala Leu Pro Lys Ile Gly Ser Ile Thr Val Tyr Phe Pro Ser Arg Lys 85 90 95
- Gln Arg Asp Ser Ser Asp Phe Asp Ile Tyr Asp Ile Gly Val Ser Gly
 100 105 110
- Leu Gly Ile Ile Ile Gly Met Ala Gly Tyr Trp Pro Ala Thr Pro Leu 115 120 125
- Val Pro Ile Asn Ser Ser Gly Ile Tyr Ile Asp Pro Val Gly Ala Asn 130 135 140
- Thr Asn Pro Asn Thr Tyr Asn Gly Ala Thr Ala Ser Phe Gly Ala Arg 145 150 155 160
- Leu Phe Val Ala Phe Val Ala Thr Gly Arg Leu Pro Asn Gly Tyr Ile 165 170 175
- Thr Ile Pro Thr Arg Gln Leu Gly Thr Ile Leu Leu Glu Ala Lys Arg
 180 185 190
- Thr Ser Leu Asn Asn Lys Gly Leu Thr Ala Pro Val Met Leu Asn Gly 195 200 205
- Gly Arg Ile Gln Val Gln Ser Gln Thr Cys Thr Met Gly Gln Lys Asn 210 215 220
- Tyr Val Val Pro Leu Asn Thr Val Tyr Gln Ser Gln Phe Thr Ser Leu 225 230 235 240
- Tyr Lys Glu Ile Gln Gly Gly Lys Ile Asp Ile His Leu Gln Cys Pro

Asp Gly Ile Asp Val Tyr Ala Thr Leu Thr Asp Ala Ser Gln Pro Val 260 265 270

Asn Arg Thr Asp Ile Leu Thr Leu Ser Ser Glu Ser Thr Ala Lys Gly
275 280 285

Phe Gly Ile Arg Leu Tyr Lys Asp Ser Asp Val Thr Ala Ile Ser Tyr 290 295 300

Gly Glu Asp Ser Pro Val Lys Gly Asn Gly Ser Gln Trp His Phe Ser 305 310 315 320

Asp Tyr Arg Gly Glu Val Asn Pro His Ile Asn Leu Arg Ala Asn Tyr 325 330 335

Ile Lys Ile Ala Asp Ala Thr Thr Pro Gly Ser Val Lys Ala Ile Ala 340 345 350

Thr Ile Thr Phe Ser Tyr Gln 355

<210> 57

<211> 844

<212> PRT

<213> Escherichia coli

<400> 57

Met Asn Ala Asn Asn Leu Ser Cys Leu Ile Tyr Cys Arg Cys Ser Leu 1 5 10 15

Leu Leu Phe Ala Ala Leu Gly Leu Thr Val Thr Asn His Ser Phe Ala
20 25 30

Ala Glu Glu Ala Glu Phe Asp Ser Glu Phe Leu His Leu Asp Lys Gly 35 40 , 45

Ile Asn Ala Ile Asp Ile Arg Arg Phe Ser His Gly Asn Pro Val Pro 50 55 60

Glu Gly Arg Tyr Tyr Ser Asp Ile Tyr Val Asn Asn Val Trp Lys Gly
65 70 75 80

Lys Ala Asp Leu Gln Tyr Leu Arg Thr Ala Asn Thr Gly Ala Pro Thr 85 90 95

Leu	Cys	Leu	Thr 100	Pro	Glu	Leu	Leu	Ser 105	Leu	Ile	Asp	Leu	Val 110	Lys	Asp

- Thr Met Ser Gly Asn Thr Ser Cys Phe Pro Ala Ser Thr Gly Leu Ser 115 120 125
- Ser Ala Arg Ile Asn Phe Asp Leu Ser Thr Leu Arg Leu Asn Ile Glu 130 135 140
- Ile Pro Gln Ala Leu Leu Asn Thr Arg Pro Arg Gly Tyr Ile Ser Pro 145 150 155 160
- Ala Gln Trp Gln Ser Gly Val Pro Ala Ala Phe Ile Asn Tyr Asp Ala 165 170 175
- Asn Tyr Tyr Gln Tyr Ser Ser Ser Gly Thr Ser Asn Glu Gln Thr Tyr 180 185 190
- Leu Gly Leu Lys Ala Gly Phe Asn Leu Trp Gly Trp Ala Leu Arg His
 195 200 205
- Arg Gly Ser Glu Ser Trp Asn Asn Ser Tyr Pro Ala Gly Tyr Gln Asn 210 220
- Ile Glu Thr Ser Ile Met His Asp Leu Ala Pro Leu Arg Ala Gln Phe 225 230 235 240
- Thr Leu Gly Asp Phe Tyr Thr Asn Gly Glu Leu Met Asp Ser Leu Ser 245 250 255
- Leu Arg Gly Val Arg Leu Ala Ser Asp Glu Arg Met Leu Pro Gly Ser 260 265 270
- Leu Arg Gly Tyr Ala Pro Ala Val Arg Gly Ile Ala Asn Ser Asn Ala 275 280 285
- Lys Val Thr Ile Tyr Gln Asn Ala His Ile Leu Tyr Glu Thr Thr Val 290 295 300
- Pro Ala Gly Pro Phe Val Ile Asn Asp Leu Tyr Pro Ser Gly Tyr Ala 305 310 315 320

- Gly Asp Leu Leu Val Lys Ile Thr Glu Ser Asn Gly Gln Thr Arg Met 325 330 335
- Phe Thr Val Pro Phe Ala Ala Val Ala Gln Leu Ile Arg Pro Gly Phe 340 345 350
- Ser Arg Trp Gln Met Ser Val Gly Lys Tyr Arg Tyr Ala Asn Lys Thr 355 360 365
- Tyr Asn Asp Leu Ile Ala Gln Gly Thr Tyr Gln Tyr Gly Leu Thr Asn 370 375 380
- Asp Ile Thr Leu Asn Ser Gly Leu Thr Thr Ala Ser Gly Tyr Thr Ala 385 390 395 400
- Gly Leu Ala Gly Leu Ala Phe Asn Thr Pro Leu Gly Ala Ile Ala Ser 405 410 415
- Asp Ile Thr Leu Ser Arg Thr Ala Phe Arg Tyr Ser Gly Val Thr Arg 420 425 430
- Lys Gly Tyr Ser Leu His Ser Ser Tyr Ser Ile Asn Ile Pro Ala Ser 435 440 445
- Asn Thr Asn Ile Thr Leu Ala Ala Tyr Arg Tyr Ser Ser Lys Asp Phe 450 455 460
- Tyr His Leu Lys Asp Ala Leu Ser Ala Asn His Asn Ala Phe Ile Asp 465 470 475 480
- Asp Val Ser Val Lys Ser Thr Ala Phe Tyr Arg Pro Arg Asn Gln Phe 485 490 495
- Gln Ile Ser Ile Asn Gln Glu Leu Gly Glu Lys Trp Gly Gly Met Tyr 500 505 510
- Leu Thr Gly Thr Thr Tyr Asn Tyr Trp Gly His Lys Gly Ser Arg Asn 515 520 525
- Glu Tyr Gln Ile Gly Tyr Ser Asn Phe Trp Lys Gln Leu Gly Tyr Gln 530 540
- Ile Gly Leu Ser Gln Ser Arg Asp Asn Glu Gln Gln Arg Arg Asp Asp

139

545					550					555					560
Arg	Phe	Tyr	Ile	Asn 565	Phe	Thr	Leu	Pro	Leu 570		Gly	Ser	Val	Gln 575	Ser
Pro	Val	Phe	Ser 580	Thr	Val	Leu	Asn	Tyr 585	Ser	Lys	Glu	Glu	Lys 590	Asn	Ser
Ile	Gln	Thr 595	Ser	Ile	Ser	Gly	Thr 600	Gly	Gly	Glu	Asp	Asn 605	Gln	Phe	Ser
Tyr	Gly 610	Ile	Ser	Gly	Asn	Ser 615	Gln	Glu	Asn	Gly	Pro 620	Ser	Gly	Tyr	Ala
Met 625	Asn	Gly	Gly	Tyr	Arg 630	Ser	Pro	Tyr	Val	Asn 635	Ile	Thr	Thr	Thr	Val 640
Gly	His	Asp	Thr	Gln 645	Asn	Asn	Asn	Gln	Arg 650	Ser	Phe	Gly	Ala	Ser 655	Gly
Ala	Val	Val	Ala 660	His	Pro	Tyr	Gly	Val 665	Thr	Leu	Ser	Asn	Asp 670	Leu	Ser
Asp	Thr	Phe 675	Ala	Ile	Ile	His	Ala 680	Glu	Gly	Ala	Gln	Gly 685	Ala	Val	Ile
Asn	Asn 690	Ala	Ser	Gly	Ser	Arg 695	Leu	Asp	Phe	Trp	Gly 700	Asn	Gly	Val	Val
Pro 705	Tyr	Val	Thr	Pro	Tyr 710	Glu	Lys	Asn	Gln	Ile 715	Ser	Ile	Asp	Pro	Ser 720
Asn	Leu	Asp	Leu	Asn 725	Val	Glu	Leu	Ser	Ala 730	Thr	Glu	Gln	Glu	Ile 735	Ile
Pro	Arg	Ala	Asn 740	Ser	Ala	Thr	Leu	Val 745	Lys	Phe	Asp	Thr	Lys 750	Thr	Gly
Arg	Ser	Leu 755	Leu	Phe	Asp	Ile	Arg 760	Met	Ser	Thr	Gly	Asn 765	Pro	Pro	Pro
/let	Ala 770	Ser	Glu	Val	Leu	Asp 775	Glu	His	Gly	Gln	Leu 780	Ala	Gly	Tyr	Val

Ala Gln Ala Gly Lys Val Phe Thr Arg Gly Leu Pro Glu Lys Gly His 785 790 795 800

Leu Ser Val Val Trp Gly Pro Asp Asn Lys Asp Arg Cys Ser Phe Val 805 810 815

Tyr His Val Ala His Asn Lys Asp Asp Met Gln Ser Gln Leu Val Pro 820 825 830

Val Leu Cys Ile Gln His Pro Asn Gln Glu Lys Thr 835 840

<210> 58

熟妆

<211> 277

<212> PRT

<213> Escherichia coli

<400> 58

Met Val Lys Cys His Thr Leu Ile Asn Arg Arg Asn Lys Cys Leu Leu 1 5 10 15

Ile Val Phe Ile Val Leu Ile Gly Trp Ile Ile Phe Arg Pro Lys Ala 20 25 30

Tyr Thr Tyr Ser Leu Asn Asp Lys Glu Lys Glu Met Leu Ile Met Leu 35 40 45

Ser Gln His Pro Glu Thr Arg Tyr Phe Gly Phe Tyr Ser Ile Glu Leu 50 55 60

Pro Ala Asp Tyr Lys Pro Thr Gly Met Val Met Phe Ile Gln Gly Ser 65 70 75 80

Ala Met Ile Pro Val Glu Thr Lys Leu Gln Tyr Tyr Pro Pro Phe Leu 85 90 95

Gln Tyr Met Thr Arg Tyr Glu Ala Glu Leu Lys Asn Thr Ser Ala Leu 100 105 110

Asp Pro Leu Asp Thr Pro Tyr Leu Lys Gln Val His Pro Leu Ser Pro 115 120 125

Pro Met Asn Gly Val Ile Phe Glu Arg Met Lys Ala Lys Tyr Thr Pro

(a)

141

130 135 140

Asp Phe Ala Arg Val Leu Asp Ala Trp Lys Trp Glu Asn Gly Val Thr 145 150 155 160

Phe Ser Val Lys Ile Glu Ala Lys Asp Gly Arg Ala Thr Arg Tyr Asp 165 170 175

Gly Ile Ser Lys Ile Ala Glu Tyr Ser Tyr Gly Tyr Asn Ile Pro Glu 180 185 190

Lys Lys Val Gln Leu Leu Thr Ile Leu Ser Gly Leu Gln Pro Arg Ala 195 200 205

Asp Asn Gln Pro Pro Ser Glu Asn Lys Leu Ala Ile Gln Tyr Ala Gln 210 215 220

Val Asp Ala Ser Leu Leu Gly Glu Tyr Glu Leu Ser Val Asp Tyr Lys 225 230 235 240

Asn Ser Asn Asn Ile Lys Ile Ser Leu Gln Thr Asp Asn Asn Ser Tyr 245 250 255

Ile Asp Ser Leu Leu Asp Ile Arg Tyr Pro Ser Asn Gly Asn Arg Ala 260 265 270

Trp Tyr Asn Ser Ile 275

<210> 59

<211> 366

. <212> PRT

<213> Escherichia coli

<400> 59

Met Leu Pro Glu Pro Val Tyr Arg Arg Trp Ile Ile Leu Leu Ile Ser 1 10 15

Met Leu Thr Val Gly Thr Leu Phe Ile Leu Ser Val Trp Asn Ser Ala

Thr Tyr Trp Asp Ile Phe Ile Tyr Gly Val Leu Pro Met Leu Phe Leu 35 40 45

1__

- Trp Leu Cys Leu Phe Gly Ile Ala Leu Asn Lys Tyr Glu Gln Ser Val 50 55 60
- Ala Ala Cys Ile Ser Trp Glu Ser Glu Arg Gln Gln Val Lys Gln Leu 65 70 75 80
- Trp Gln His Trp Ser Gln Lys Gln Leu Ala Ile Val Gly Asn Val Leu 85 90 95
- Phe Thr Pro Glu Glu Lys Gly Met Ser Val Leu Leu Gly Pro Gln Glu 100 105 110
- Glu Ile Pro Ala Tyr Pro Lys Lys Ala Arg Pro Leu Phe Ser Ala Ser 115 120 125
- Arg Tyr Ser Leu Ser Ser Ile Phe His Asp Ile His Gln Gln Leu Thr 130 135 140
- Gln Gln Phe Pro Asp Tyr Arg His Tyr Leu His Thr Ile Tyr Val Leu 145 150 155 160
- Gln Pro Glu Lys Trp Arg Gly Glu Thr Val Arg Gln Ala Ile Phe His 165 170 175
- Gln Trp Asp Leu Val Pro Glu Arg Thr Asn Thr Leu Asn Gln Ile Gln
 180 185 190
- Ser Leu Tyr Asp Glu Arg Phe Asp Gly Leu Ile Leu Val Val Cys Leu 195 200 205
- Gln Asn Trp Pro Glu Asn Lys Pro Glu Asp Thr Ser Glu Leu Val Ser 210 215 220
- Ala Gln Leu Ile Ser Ser Ser Phe Val Arg Gln His Gln Ile Pro 225 230 235 240
- Val Ile Ala Gly Leu Gly Arg Val Met Pro Leu Glu Pro Glu Glu Leu 245 250 255
- Glu His Asn Leu Asp Val Leu Phe Glu Tyr Asn Gln Leu Asp Asn Lys 260 265 270
- Gln Leu Gln His Val Trp Val Ser Gly Leu Asp Glu Gly Thr Ile Glu

143

275 280 285

Asn Leu Met Gln Tyr Ala Glu Gln His Gln Trp Ser Leu Pro Lys Lys 290 295 300

Arg Pro Leu His Met Ile Asp His Ser Phe Gly Pro Thr Gly Glu Phe 305 310 315 320

Ile Phe Pro Val Ser Leu Ala Met Leu Ser Glu Ala Ala Lys Glu Thr 325 330 335

Glu Gln Asn His Leu Ile Ile Tyr Gln Ser Ala Gln Tyr Ala Gln Lys 340 345 350

Lys Ser Leu Cys Leu Ile Thr Arg Lys Leu Tyr Leu Arg Thr 355 360 365

<210> 60

<211> 260

<212> PRT

<213> Escherichia coli

<400> 60

Met Leu Asn Arg Lys Leu Asn Ile Arg Leu Arg His Ser Leu Asn Ser 1 10 15

His Cys Ile Pro Ser Ile Ile Ile Asn Asn Thr Val Arg Ser Phe Gln 20 25 30

Arg Ser Val Met Asn Thr Arg Ala Leu Phe Pro Leu Leu Phe Thr Val 35 40 45

Ala Ser Phe Ser Ala Ser Ala Gly Asn Trp Ala Val Lys Asn Gly Trp 50 55 60

Cys Gln Thr Met Thr Glu Asp Gly Gln Ala Leu Val Met Leu Lys Asn 65 70 75 80

Gly Thr Ile Gly Ile Thr Gly Leu Met Gln Gly Cys Pro Asn Gly Val 85 90 95

Gln Thr Leu Leu Gly Ser Arg Ile Ser Ile Asn Gly Asn Leu Ile Pro 100 105 110 Thr Ser Gln Met Cys Asn Gln Gln Thr Gly Phe Arg Ala Val Glu Val 115 120 125

Glu Ile Gly Gln Ala Pro Glu Met Val Lys Lys Ala Val His Ser Ile 130 135 140

Ala Glu Arg Asp Val Ser Val Leu Gln Ala Phe Gly Val Arg Met Glu 145 150 155 160

Phe Thr Arg Gly Asp Met Leu Lys Val Cys Pro Lys Phe Val Thr Ser 165 170 175

Leu Ala Gly Phe Ser Pro Lys Gln Thr Thr Thr Ile Asn Lys Asp Ser 180 185 190

Val Leu Gln Ala Arg Gln Ala Tyr Ala Arg Glu Tyr Asp Glu Glu 195 200 205

Thr Thr Glu Thr Ala Asp Phe Gly Ser Tyr Glu Val Lys Gly Asn Lys 210 215 220

Val Glu Phe Glu Val Phe Asn Pro Glu Asp Arg Ala Tyr Asp Lys Val 225 230 235 240

Thr Val Thr Val Gly Ala Asp Gly Asn Ala Thr Gly Ala Ser Val Glu 245 250 255

Phe Ile Gly Lys 260

<210> 61

<211> 385

<212> PRT <213> Escherichia coli

<400> 61

Val Val Ile Ile Asn Ser Thr Ile Leu Ser Gly Ala Gly Ala Ile Pro 1 5 10 15

Ser Leu Thr Ser Leu Leu Pro Asp Ile Arg Lys Met Leu Leu Val Thr 20 25 30

Asp Arg Asn Ile Ala Gln Leu Asp Gly Val Gln Gln Ile Arg Ala Leu 35 40 45

Leu	Glu	Lys	His	Cys	Pro	Gln	Val	Asn	Val	Ile	Asp	Asn	Val	Pro	Ala
	50					55					60				

- Glu Pro Thr His His Asp Val Arg Gln Leu Met Asp Ala Pro Gly Asp 65 70 75 80
- Ala Ser Phe Asp Val Val Val Gly Ile Gly Gly Gly Ser Val Leu Asp 85 90 95
- Val Ala Lys Leu Leu Ser Val Leu Cys His Pro Gln Ser Pro Gly Leu
 100 105 110
- Asp Ala Leu Leu Ala Gly Glu Lys Pro Thr Gln Arg Val Gln Ser Trp 115 120 125
- Leu Ile Pro Thr Thr Ala Gly Thr Gly Ser Glu Ala Thr Pro Asn Ala 130 135 140
- Ile Leu Ala Ile Pro Glu Gln Ser Thr Lys Val Gly Ile Ile Ser Gln 145 150 155 160
- Val Leu Pro Asp Tyr Val Ala Leu Phe Pro Glu Leu Thr Thr Ser 165 170 175
- Met Pro Ala His Ile Ala Ala Ser Thr Gly Ile Asp Ala Leu Cys His 180 185 190
- Leu Leu Glu Cys Phe Thr Ala Thr Val Ala Asn Pro Val Ser Asp Asn 195 200 205
- Ala Ala Leu Thr Gly Leu Ser Lys Leu Phe Arg His Ile Gln Pro Ala 210 215 220
- Val Asn Asp Pro Gln Asp Leu Arg Ala Lys Leu Glu Met Leu Trp Ala 225 230 235 240
- Ser Tyr Tyr Gly Gly Val Ala Ile Thr His Ala Gly Thr His Leu Val 245 250 255
- His Ala Leu Ser Tyr Pro Leu Gly Gly Lys Tyr His Leu Pro His Gly 260 265 270

Val Ala Asn Ala Ile Leu Leu Ala Pro Cys Met Ala Phe Val Arg Pro 275 280 285

Trp Ala Val Glu Lys Phe Ala Arg Val Trp Asp Cys Ile Pro Asp Ala 290 295 300

Glu Thr Ala Leu Ser Ala Glu Glu Lys Ser His Ala Leu Val Thr Trp 305. 310 315 320

Leu Gln Ala Leu Val Asn Gln Leu Lys Leu Pro Asn Asn Leu Ala Ala 325 330 335

Leu Gly Val Pro Pro Glu Asp Ile Ala Ser Leu Ser Glu Ala Ala Leu 340 345 350

Asn Val Lys Arg Leu Met Asn Asn Val Pro Cys Gln Ile Asp Leu Gln 355 360 365

Asp Val Gln Ala Ile Tyr Gln Thr Leu Phe Pro Gln His Pro Phe Lys 370 375 380

Glu 385

<210> 62

<211> 105

<212> PRT

<213> Escherichia coli

<400> 62

Met Asn Ile Arg Lys Leu Phe Cys Pro Gly Asn Thr Pro Arg Ile Leu 1 5 10 15

Leu Phe Leu Phe Phe Phe Val Val Ser Ala Ile Thr Thr Ile Ala Cys 20 2.5 30

Gly Tyr Thr Glu Lys Asn Ala Thr Gly Asn Val Leu Leu Leu Phe Leu 35 40 45

Leu Leu Leu Ala His Arg Asn Thr Leu Thr Ser Ile Thr Ala Leu 50 55 60

Leu Phe Leu Phe Cys Cys Ala Leu Tyr Ala Pro Ala Gly Met Thr Tyr 65 70 75 80

(

Gly Lys Ile Asn Asn Ser Phe Ile Val Ala Leu Leu Gln Thr Thr 90

Asp Glu Ala Ala Glu Phe Thr Gly Met 100

<210> 63 <211> 147 <212> PRT <213> Escherichia coli

Met Asn Ile Gln Ala Ile Lys Glu Met Val Asn Leu Ile Cys Ser Phe 5

Leu Phe Ile Phe Phe Leu Ser Ser Ala Phe Val Ser Phe Gly Cys Tyr 20 25 30

Ala Ile Tyr Glu Leu Phe Leu Trp Asn Asp Ile Ile Val Tyr Ser Trp 35 40

Gly Tyr Ile Leu Ile Val Phe Leu Pro Phe Thr Leu Tyr Val Met Ser 50

Phe Glu Ile Leu Phe Phe Ala Ile Ser Gly Arg Arg Leu Ser Lys Val 75

Thr Met Val Arg Leu Trp Leu Ile Ile Lys Ile Ile Ile Ala Phe Ser

Ile Cys Ala Val Leu Ile Phe Ser Ser Ile Tyr Lys Lys Glu Leu Leu 100 105 . 110

Ser Arg Asn Tyr Ile Ala Cys Ser Gly Ile Pro Ser Gly Trp Met Pro 115

Gly Leu Ala Thr Lys Tyr Val Lys Glu Lys Ser Leu Cys Glu Lys Asn 130 135

Gly Asn Asn 145

<210> 64 <211> 178

0207455242 1 -

<2	21	2	>	PRT
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<213> Escherichia coli

<400> 64

Met Phe Pro Ile Arg Phe Lys Arg Pro Ala Leu Leu Cys Met Ala Met 1 5 10 15

Leu Thr Val Val Leu Ser Gly Cys Gly Leu Ile Gln Lys Val Val Asp 20 25 30

Glu Ser Lys Ser Val Ala Ser Ala Val Phe Tyr Lys Gln Ile Lys Ile 35 40 45

Leu His Leu Asp Phe Phe Ser Arg Ser Ala Leu Asn Thr Asp Ala Glu 50 55 60

Asp Thr Pro Leu Ser Thr Met Val His Val Trp Gln Leu Lys Thr Arg 65 70 75 80

Glu Asp Phe Asp Lys Ala Asp Tyr Asp Thr Leu Phe Met Gln Glu Glu 85 90 95

Lys Thr Leu Glu Lys Asp Val Leu Ala Lys His Thr Val Trp Val Lys 100 105 110

Pro Glu Gly Thr Ala Ser Leu Asn Val Pro Leu Asp Lys Glu Thr Gln 115 120 125

Phe Val Ala Ile Ile Gly Gln Phe Tyr His Pro Asp Glu Lys Ser Asp 130 135 140

Ser Trp Arg Leu Val Ile Lys Arg Asp Glu Leu Glu Ala Asp Lys Pro 145 150 155 160

Arg Ser Ile Glu Leu Met Arg Ser Asp Leu Arg Leu Leu Pro Leu Lys 165 170 175

Asp Lys

<210> 65

<211> 209

<212> PRT

<213> Escherichia coli

<400> 65

- Met Phe Leu Lys Arg Lys Trp Tyr Tyr Ala Val Thr Thr Ser Val Val 1 5 10 15
- Ile Thr Leu Cys Gly Gly Gly Tyr Tyr Met Tyr Arg Gln Glu Tyr Gln 20 25 30
- Met Val Val Thr Val Pro Thr Ala Asp Ala Asn Asp Pro Asn Trp Pro 35 40 45
- Asn Lys Arg Ile Gln Phe Asp Thr Ser Glu Trp Leu Gln Gln Leu Gln 50 55 60
- Tyr Ile Lys Ile Asp Asp His Tyr Ile Leu Asn Thr Gln Tyr Thr Pro 65 70 75 80
- Ile Ala Asn Leu Asp Asp Phe Gly Ile Thr Leu Lys Leu Gln Asn Ala 85 90 95
- Leu Asn Gly Ser Asp Lys Arg Leu Pro Ala Leu Tyr Gly Leu Ala Glu
 100 105 110
- Met Asp Ala Gln Lys Phe Lys Asp Leu Met Arg Gly Lys Ile Lys Cys
 115 120 125
- Glu Tyr Leu Arg Thr Thr Phe Asp Ala Glu Thr Leu Lys Pro Val Asn 130 135 140
- Asp Tyr Phe Leu Ile Ser Phe Thr Tyr Lys Asp Lys Trp Tyr Glu Phe 145 150 155 160
- Glu Thr Glu Arg Lys Ile Ser Lys Thr Ser Asp Asp Gly Tyr Phe Leu 165 170 175
- Trp Ala Phe Asp Asn Thr Val His Glu Ala Gly Tyr Trp His Asn Thr 180 185 190
- Asp Pro Ala Ala Tyr Ser Tyr Arg Asp Tyr Gln Asn Gly Lys Ala Val

Lys

		150													
<21: <21: <21:	0 > l > 2 > 3 >	424 PRT Esche	eric	nia (coli										•
Met 1	Asp	Ile	Trp	Arg 5	Gly	His	Ser	Phe	Leu 10	Met	Thr	Ile	Ser	Ala 15	Arg
Phe	Arg	Gln	Tyr 20	Val	Phe	Ser	Leu	Met 25	Ser	Ile	Leu	Leu	Gln 30	Glu	Arg

Lys Met Asn Ile Phe Thr Leu Ser Lys Ala Pro Leu Tyr Leu Leu Ile

Ser Leu Phe Leu Pro Thr Met Ala Met Ala Ile Asp Pro Pro Glu Arg

Glu Leu Ser Arg Phe Ala Leu Lys Thr Asn Tyr Leu Gln Ser Pro Asp 70

Glu Gly Val Tyr Glu Leu Ala Phe Asp Asn Ala Ser Lys Lys Val Phe 90

Ala Ala Val Thr Asp Arg Val Asn Arg Glu Ala Asn Lys Gly Tyr Leu

Tyr Ser Phe Asn Ser Asp Ser Leu Lys Val Glu Asn Lys Tyr Thr Met 120

Pro Tyr Arg Ala Phe Ser Leu Ala Ile Asn Gln Asp Lys His Gln Leu 135

Tyr Ile Gly His Thr Gln Ser Ala Ser Leu Arg Ile Ser Met Phe Asp

Thr Pro Thr Gly Lys Leu Val Arg Thr Ser Asp Arg Leu Ser Phe Lys 165 170

Ala Ala Asn Ala Ala Asp Ser Arg Phe Glu His Phe Arg His Met Val 180 185

Tyr Ser Gln Asp Ser Asp Thr Leu Phe Val Ser Tyr Ser Asn Met Leu 200 205

Lys	Thr	Ala	Glu	Gly	Met	Lys	Pro	Leu	His	Lys	Leu	Leu	Met	Leu	Asp
	210					215					220				

Gly Thr Thr Leu Ala Leu Lys Gly Glu Val Lys Asp Ala Tyr Lys Gly 225 230 235 240

Thr Ala Tyr Gly Leu Thr Met Asp Glu Lys Thr Gln Lys Ile Tyr Val 245 250 255

Gly Gly Arg Asp Tyr Ile Asn Glu Ile Asp Ala Lys Asn Gln Thr Leu 260 265 270

Leu Arg Thr Ile Pro Leu Lys Asp Pro Arg Pro Gln Ile Thr Ser Val 275 280 285

Gln Asn Leu Ala Val Asp Ser Ala Ser Asp Arg Ala Phe Val Val 290 295 300

Phe Asp His Asp Asp Arg Ser Gly Thr Lys Asp Gly Leu Tyr Ile Phe 305 310 315 320

Asp Leu Arg Asp Gly Lys Gln Leu Gly Tyr Val His Thr Gly Ala Gly 325 330 335

Ala Asn Ala Val Lys Tyr Asn Pro Lys Tyr Asn Glu Leu Tyr Val Thr 340 345 350

Asn Phe Thr Ser Gly Thr Ile Ser Val Val Asp Ala Thr Lys Tyr Ser 355 360 365

Ile Thr Arg Glu Phe Asn Met Pro Val Tyr Pro Asn Gln Met Val Leu 370 375 380

Ser Asp Asp Met Asp Thr Leu Tyr Ile Gly Ile Lys Glu Gly Phe Asn 385 390 395 400

Arg Asp Trp Asp Pro Asp Val Phe Val Glu Gly Ala Lys Glu Arg Ile 405 410 415

Leu Ser Ile Asp Leu Lys Lys Ser 420

<210> 67						
<211> 489 <212> DNA					٠	
	nerichia col	.i				
-100> 67					atttaagaa	60
atgaaactga	aagctattat	attggccacc	ggtcttatta	actgtattgt	acticoagoa	80
caggcagtgg	atacgacgat	tactgtgacg	ggtaatgttt	tgcaaagaac	atgtaatgta	120
ccagggaatg	tggatgtttc	tttgggtaat	ctgtatgtat	cagactttcc	caatgcagga	180
agtggatctc	catgggttaa	ttttgatctg	tctctcaccg	gatgccagaa	tatgaatact	240
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Seq ID 134

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Seq ID 146

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Seq ID 148

Seq ID 149

Seq ID 150

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Seq ID 151

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AAACGCATGGTGCAGGTGATCAACGGTCAGCCGCCGCAAATCATCACGGCAGAAAACAACCCGCAGATGTTCCAGTTTAA
CCACCTGCTGCGCGCGCTGTTCCAGGCCGATCGCAAAGTGCTGGAACAAACTTCCGCGTCGAATTTGCTGACAAAGGCG
AAGGCCGCTGGACGCCTGACGCCGACCACCACGCCGCTGGATAAAATTTTCAACACCATCGATCTCACCGGGAAA
ACCTATCTGGAGAGCATTCAACTTAATGATAAACAGGGCGATCGCACCGATATTGCTCTTACCCAACATCAACTGACGCC
AGCGCAACTGACCGATGACGAACACCAACGTTTTGCCGCCCAG

Seq ID 152

TGATAGCACGGTATCAACTGATCCGGTTACGCTGAATACAGAGAAGACGACTCTGGATCAAGATGTTGTTATTAACGGTG ATAACAAGATTACAGCCGTAACAATTGAAACGTCAGATTCAGATAAAGACCTTAATGTTACTTTTGGCGGTCACGATATT ACCGCCGCATCAACGGTAAACCAAGATTTCGTTGAAGGTGTAAAAGTTAGTGGTAACAAAAATGTTGTGATTAATGCTAC AGACTCCACCATCACAGCTCAAGGTGAAGGCACCTATGTCCGGACTGCAATGGTCATTGATTCAACTGGCGATGTTGTTG $\tt TTAATGGCGGTAATTTCGTTGCAAAAATGAAAAAGGTAGTGCGACAGGGATATCTCTGGAAGCGACCACGGGAAATAAT$ TTAACGCTCAATGGTACAACCATAAATGCTCAAGGTAATAAGAGTTACAGCAACGGCTCTACGGCAATTTTTGCTCAAAA GGGTAATTTGTTGCAGGGTTTTGACGGTGATGCAACCGACAACATCACCCTTGCTGACTCAAATATTATTAATGGCGGGA TTGAAACAATAGTTACTGCCGGGAATAAGACGGGAATTCATACAGTCAACCTGAATATTAAGGATGGCTCAGTAATTGGG GCGGCTAATAATAAACAAACAATTTATGCCTCTGCTTCGGCACAAGGCGCAGGTTCAGCAACGCAAAATTTAAATTTGTC TGTTGCTGATTCAACCATCTACTCTGATGTCCTGGCCCTTTCTGAAAGCGAGAATTCAGCCAGTACCACAACAAATGTAA $\tt ATATGAACGTTGCCCGCTCTTACTGGGAAGGTAATGCTTATACCTTCAATAGCGGCGATAAAGCGGGTAGTGATCTGGAT$ $\tt ATAAATCTTTCCGATAGTTCAGGAAAGGCAAAGTTTCAGGGGCAGGAGATGCCAGTGTATCTCTGCAAAACGGGTC$ ${\tt TGTCTGGAATGTTACGGGTTCCTCAACTGTTGATGCTCTGGCAGTAAAAGACAGTACGGTTAATATCACGAAGGCTACAG$ ${ t TCAATACTGGCACGTTTGCTTCAAAACGGCACTCTGATTGTTGATGCCTCTTCTGAAAACACTCTGGATATCAGCGGT$ CAAAGACAGCACTCTAAAAGCCACAGGCACAACGGAAGGTGGTCTGTATCAATATGACCTGACACAGGGAGCTGATGGTA ${ t ACTTTTATTTCGTAAAAAACACGCATAAAGCATCCAACGCCAGCTCCGTGATTCAGGCAATGGCAGCTGCTCCGGCTAAC$ GTCGCTAATCTGCAGGCTGACACGCTCTCCGCCCGTCAGGATGCTGTCCGTCTGAGCGAAAATGACAAGGGTGGCGTATG GATTCAGTACTTTGGCGGTAAACAGAAACATACCACCGCGGGAAATGCATCCTATGACCTGGATGTAAATGGTGTAATGC TGGGTGGTGATACCCGCTTCATGACTGAAGATGGTAGCTGGCCGGTGTGGCGATGTCTTCTGCGAAAGGTGACATG ${ t ACTACCATGCAGAGCAAAGGTGACACTGAAGGTTACAGCTTCCACGCTTACCTGAGCCGCCAGTATAACAACGGTATCTT}$ CATTGATACTGCTGCACAGTTTGGTCACTACAGCAACACGGCAGATGTTCGCCTGATGAATGGTGGCGGTACCATCAAAG ${ t CTGACTTTAACACCAATGGTTTTGGTGCGATGGTTAAAGGCGGTTACACATGGAAAGACGGTAATGGCCTGTTTATTCAG$

CCATATGCCAAACTGTCTGCTCTGACTCTGGAAGGTGTGGATTATCAACTCAACGGCGTGGACGTTCATTCTGACAGCTA
TAACTCTGTGCTGGGTGAGGCCGGTACGCGCGTGGGTTATGACTTCTGCTGTGGGCAACGCGACCGTTAAACCTTATCTGA
ATCTGGCCGCACTGAACGAATTCTCTGATGGCAACAAAGTCCGTCTGGGTGATGAGGTCTGTCAATGCCAGCATTGACGGT
GCAGCATTCCGCGTGGGTGCAGGTGTACAAGCTGATATCACCAAAAACATGGGAGCATATGCAAGCCTTGACTACACCAA
AGGTGACGACATTGAGAACCCGCTACAGGGTGTAGTTGGTATCAATGTGACCTGG

Seq ID 153

 ${ t ATGTCACGTCGCAATTTACCTCGTTGCGTTTGAGTTTGTTGGCTTTTGGCTGTTTCTGCCACCTTTGCCAACGTTTGCTTT$ TGCTACTGAAACCATGACCGTTACGGCAACGGGGAATGCACGTAGTTCCTTCGAAGCGCCTATGATGGTCAGCGTTATCG ${ t ACACTTCCGCTCCTGAAAATCAAACTGCTACTTCAGCCACTGATTTGCTGCGTCATGTTCCTGGAATTACTCTTGATGGT$ ACCGGACGAACCAACGGTCAGGATGTAAATATGCGTGGCTATGATCATCGCGGCGTGCTGGTTCTTGTCGATGGTGTTCG GAAGGACAAAGCAGTGGTTTTCGTGTCTTTGGTACTGGCGGCACGGGGGACCATAGCCTGGGATTAGGCGCGAGCGCGTT ${ t TGGGCGAACTGAAAATCTGGATGGTATTGTGGCCTGGTCCAGTCGCGATCGGGGTGATTTACGCCAGAGCAATGGTGAAA}$ ${\tt CCGCGCCGAATGACGAGTCCATTAATAACATGCTGGCGAAAGGGACCTGGCAAATTGATTCAGCCCAGTCTCTGAGCGGT$ ${ t TTAGTGCGTTACTACAACAACGACGCGCGTGAACCAAAAAATCCGCAGACCGTTGAAGCTTCTGATAGCAGCAACCCGAT$ GGTCGATCGTTCAACAATTCAACGCGATGCGCAGCTTTCTTATAAACTCGCCCCGCAGGGTAACGACTGGTTAAATGCAG ATGCAAAAATTTACTGGTCGGAAGTCCGTATTAATGCGCAAAACACGGGGGGGTTCAGGCGAGTATCGTGAACAGATAACA AAAGGAGCAAGGCTGGAGAACCGTTCCACTCTATTTGCCGACAGTTTCGCTTCTCACTTACTGACATATGGCGGTGAGTA GGCTACAAAGATGTTGATGCCGACAAATGGTCATCTCGTGCGGGGATGACTATCAACCCGACCAACTGGCTGATGTTATT ${ t TGGCTCATATGCTCAGGCATTCCGCGCCCCGACGATGGGCGAAATGTATAACGATTCTAAACACTTCTCGATTGGTCGCT$ ${ t TCTATACCAACTATTGGGTGCCAAACCCGAACTTACGTCCGGAAACTAACGAAACTCAGGAGTACGGTTTTGGGCTGCGT$ ${ t TTTGATGACCTGATGTTGTCCAATGATGCTCTGGAATTTAAAGCCAGCTACTTTGATACCAAAGCGAAAGATTATATCTC$ ${ t CACGACCGTCGATTTCGCGGCGGCGACAACTATGTCGTATAACGTCCCGAACGCCAAAATCTGGGGCTGGGATGTGATGA}$ ${\tt CGAAATATACCACTGATCTGTTTAGCCTTGATGTGGCCTATAACCGTACCCGCGGCAAAGACACCGATACCGGGGAATAT$ ${\tt TCAGTTATCAAGGGCAGCAGGCGCTCAAAGGCATGACCACTACTCTGGTATTGGGCAACGCCTTCGATAAAGAGTACTGG}$ TCGCCGCAAGGCATCCCACAGGATGGTCGTAACGGAAAAATTTTCGTGAGTTATCAATGG

Seq ID 154

 $\tt ATGAGGGATGAAATGTTATATATATATCCTTGTCGAATTTATATCCTTTCCACTCTGTCATTATGCATTTCTGGGATAGT$ ${\tt TTCTACTGCAACCGCAACTTCTTCAGAAACAAAATCAGCAACGAAGAGACGCTCGTCGTGACCACGAATCGTTCGGCAA}$ GCAACCTTTGGGAAAGCCCGGCGACTATACAGGTTATTGACCAACAACATTGCAGAACTCCACCAATGCCTCCATAGCC GATAATTTGCAGGACATCCCCGGAGTAGAGATAACAGACAACTCCTTGGCAGGCCGTAAACAAATCCGCATTCGTGGCGA ${\tt AGCATCCTCCCGTGTTTTAATTCTCATTGATGGTCAGGAGGTAACTTATCAGCGCGCGGAGATAATTATGGTGTGGGAC}$ $\tt TGTTGATAGATGAGTCTGCGCTGGAGCGTGTTGAGGTAGTGAAAGGTCCATATTCCGTACTGTACGGTTCACAGGCAATT$ ${\tt GGCGGTATTGTTAACTTCATAACCAAAAAGGGAGGTGACAAACTTGCATCTGGAGTTGTGAAAGCTGTTTATAATTCCGC}$ AACAGCAGGCTGGGAAGAATCAATCGCGGTCCAGGGGAGCATCGGTGGATTTGATTATCGCATCAACGGTAGTTATTCTG ATCAGGGCAATCGTGATACGCCGGATGGACGTCTGCCGAATACCAACTATCGTAACAATAGTCAGGGTGTATGGTTGGGT TATAACTCCGGAAACCATCGTTTTGGCCTCTCGCTTGATCGCTACAGACTCGCGACGCAAACTTACTATGAGGATCCAGA $\tt CGGAAGCTATGAGGCATTTAGTGTCAAAATACCTAAACTTGAACGAGAGAAAGTTGGGGTATTCTATGACACAGACGTGG$ ACGGTGACTATCTAAAAAAAATTCATTTCGACGCGTATGAGCAGACCATCCAGCGCCAATTTGCCAACGAAGTAAAAACG ACACAGCCTGTTCCCAGTCCGATGATTCAGGCTCTGACCGTTCATAACAAGACTGACACCCATGATAAGCAATACACTCA TCAGCCAAAGGTCCGGTGGCATGACCTCAAGCAAATCTCTGACCGGCTTCATTAATAAGGAAACACGAACTCGCTCCTAT TATGAGTCAGAGCAAAGTACAGTCTCACTATTCGCACAAAATGACTGGCGATTCGCCGATCACTGGACATGGACAATGGG ${ t AGTTCGCCAATACTGGCTTTCTTCAAAGTTGACGCGTGGTGACGGAGTATCATATACCGCAGGCATTATAAGCGATACCT}$ ${ t CACATACGGAAATCCTGATCTTAAGGCTGAACACTCCAATAACTTTGAATTAGGTGCACGATATAATGGTAATACGTGGC}$ ${\tt TGATTGACAGCGCAGTTTACTACTCAGAAGCTAAAGATTATATTGCAAGTCTGATCTGTGATGGCAGTATAGTTTGCAATTGTAATTGCAATTGCAATTGCAATTGCAATTGCAATTGCAATTGCAATTGCAATTGAATTGCAATTGCAATTGAATTGCAATTGCAATTGTAATT$ GGTAACACCAACTCCTCCCGTAGTAGCTACTATTATTATGACAATATTGATCGGGCAAAAACATGGGGACTGGAAATAAG CGCGGAATATAATGGCTGGGTTTTCTCGCCATATATCAGTGGCAATTTAATTCGTCGGCAATATGAAACTTCAACATTAA AAACAACTAATACAGGAGAACCAGCGATAAACGGACGTATAGGGCTGAAACATACTCTTGTGATGGGTCAGGCCAACATA ACAAACGCTACCGTACAGCACATGAAACTATTCCTGCAGCAGGTTTTAATGCAGCTATAGGTTTTGTATGGAATTTC

Seq ID 155

ATGCGTAAAGTTTGTGCAGTCATTTTGTCCGCAGCCATCTGTCT
GTCCGTATCCGGTGCGCCTGCATGGGCGTCTGAACATCAGTCCACACTGAGCGCGGGGTA
TCTTCATGCCCGTACGAACGCTCCCGGCAGCGATAATCTGAACGGGATTAACGTGAAATA
CCGTTATGAGTTTACGGACGCGCTGGGGCTGATTACGTCCTTCAGTTATGCCAATGCTGA
GGATGAGCAAAAAACGCACTACAGCGATACCCGCTGGCATGAAGATTCCGTGCGTAACCG
CTGGTTCAGCGTGATGGCGGGGCCGTCTGTACGCGTGAATGATGGTTCAGCGCGTAATC
GATGGCGGGTGTGGCTTACAGCCGTGTGTCGACTTTCTCCGGGGATTATCTCCGCGTAAC
TGACAACAAGGGGAAAACGCACGATGTGCTGACCGGAAGTGATGACGGTCGCCACAGCAA
CACGTCTCTGGCGTGGGGGGCCTGCCGTGCAGTTTAACCCGAACCGAATCCGTGACCATTGA
CCTTGCTTATGAAGGTTCCGGTAGTGGCGACTGGCGAACGGATGCATTTATTGTTGGTAT
CGGATACCGTTTCTGA

Seq ID 156

ATGAAAAATCGACATTATCTTTAGCCATCGGTTTATTATTGGCATGTAGTACCGGTATGGCAAAAACACAGCATTTAAC GCTGGAACACGCCTGGAAGCGGCAGAAATGCGGGCAGCAAAAGCAGAGGGGCAGGTTAAACAGCTTCAGACACAACAAG ${\tt AACGCCACCCGCCTAATCTCCTGCTTTCAGGGTATGGCGATTTAAAAATCTACGGTGACGTAGAATTTAATATGGATGC}$ $\tt GTATTCTGTTAGGTTTTGATGGTATGCGAAAACTGGATAATGGCTATTTCGCTGGGTTCTCCGCACAACCGCTGGGGGAT$ ${ t ATGCACGGTTCAGTAAATATCGATGATGCGGTTTTCTTCTTTGGCAAAGAAAACGACTGGAAGGTCAAAGTAGGCCGTTT$ TGAAGCCTACGATATGTTCCCGCTGAATCAGGATACCTTTGTTGAACATTCCGGTAATACTGCGAACGATCTTTATGACG ATGGCAGCGGTTATATCTATATGATGAAAGAGGGCCGCGGACGTTCTAACGCTGGCGGTAATTTCCTCGTCAGCAAACAA CGATATGGAACAGCAGAAAAATGTTGCTTATCTGCGTCCGGTAATTGCCTGGTCGCCGACGGAAGAATTCACCGTTTCCG ${ t CAGCGATGGAAGCGAATGTGGTAAATAATGCTTATGGTTATACCGATAGCAAGGGTAATTTTGTCGATCAGTCCGATCGT}$ ACCGGTTATGGCATGAGTATGACCTGGAATGGCCTGAAAACCGATCCGGAAAATGGCATCGTGGTTAATCTTAATACCGC CTATTTAGATGCTAATAATGAAAAAGATTTCACGGCAGGGATTAACGCGCTGTGGAAACGTTTCGAGCTGGGTTATATCT ${ t ATGCACATAATAAGATTGATGAATTTAGTGGCGTGGTTTGTGATAACGATTGCTGGATTGATGATGAAGGAACATACAAC$ ATTCACACCATTCATGCGTCTTATCAGTTCGCTAATGTGATGGATATGGAGAACTTTAATATTTACCTCGGCACGTATTA $\tt CTCCATTCTGGATAGCGACGGCGATAAGATACACGGCGACGATAGTGATGACCGTTACGGCGCACGCGTTCGCTTTAAAT$ ACTTCTTC

Seq ID 157

Seq ID 158

0207455240

 ${\tt TGGGTAACAGCTCGCCAACCTGGCCTCTGGTGGAGACGACGCCGTATTTTACTCGCCGCCTCTTCCCGGAAGTCCTG}$ $\tt CTGGCTGAGCCGAACCTGGCGGGTGAAAACAGCGTCTGGCTGAACAGCTCCCGGCGCAGGCTGACCGCCTTTTCCACCTG$ ${\tt TGGCACAAGCTAAAGCCTTTATGGACGTACCACCACCGCAGGGAACGGATGAATTCGGCAATCTGCAATTGCCATTGCTT}$ ${\tt AACCCGGTACGCGATGCCACCCTGGCCTATGGTGATTATCGCGATCACGGTTTTCTGGCGGATATGGGATTGTACCAGGG}$ TGATCCGGGATCTAAACATTGCCCCGCCAGAGAGAGCGAAGAAAGCTCGCTGTGCTGCGCGTAGTGCGCATGATGGAAGAC AAAAGTGGGCGCAACAACGAGGCGGTAAAACAGTACATGGCACGGCGCTGGAGCAATGAATTTCACGGCCAGCGCGATAT ${ t ATGCTGTCAGCCGCTGGACCCCCTATGATAAACCGATCATTAATGCGCAGCAGGAACTGAGCAAGCTGCCCATATACCAG$ CGTGTCTACCAGACCCTGCGCACCAAAGCATTAAGCGTGTTGCCCGCCGATTTGAATTTGCGCGACCAGGTTGGTCCCAC ${ t CTTCGACAACGTGTTCGTCGCCGGTAATGATGAAAAACTGGTGATCCCGCAGTTCCTCACCCGCTATGGACTGCAAAGCT$ TACAGCGAGGCCGACCGTGAAGAGATCCAGCGCCATATCACCGAACAGTACATCAGTGACTATACCGCCACCTGGCGTGC CGGAATGGATAACCTCAACGTCCGTGACTATGAGGCCATGTCGGCGCTGACCGACGCGCTGGAGCAGATTATCAGCGGCG ATCAGCCATTCCAGCGTGCGCTGACGGCGCTGCGCGATAATACCCACGCGCTGACGCTCTCCGGCAAACTGGATGATAAG ${\tt ACTGGAGGAGCAAAAGGACAAGGCGAGTACGGCCGTGTACCAGCAACTGACCGAGCTGCACCGTTACCTGCTGG}$ ${\tt CGATCCAGAACTCGCCAGTGCCGGGGAAATCGGCGCTGAAAGCAGTACAGCTACGGCTGGATCAAAACAGCAGCGATCCA}$ TTGCCGATAACTATCCGTTTAATCCGCGCGCCACACAGGATGCCTCACTGGATTCGTTTGAACGTTTCTTTAAACCGGAT GGCATTCTGGACAATTTCTACAAGAACAACCTGCGCCTGTTCCTTGAAAACGATCTGACCTTTGGCGACGACGGCAGAGT ${\tt TGGGCGCACAGTTTGCCGTGGAAACCGTATCGCTTTCCGGCAATAAGCGGCGCAGCGTACTTAACCTGGACGGCCAGTTA}$ GACGCTGATTGGCACCAGCGGCAGAGCACCGCGCAGTATCGCGTTCAGTGGACCGTGGGCGCAGTTCCGCCTGTTCGGCG CGGGCCAGTTGACCAATGTGACCAGTGACACCTTTAACGTGCGCTTTAACGTGGACGGCGCGCAATGGTTTACCAGGTG CATGTGGATACCGAAGATAACCCGTTCACCGGCGGTCTGTTCAGCCTGTTCCGGTTTACCGGATACGTTGTAT



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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
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Published:

with international search report

(88) Date of publication of the international search report: 25 March 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: EXPEC-SPECIFIC PROTEINS, GENES ENCODING THEM AND USES THEREOF

(57) Abstract: The invention relates to isolated antigenic polypeptides obtainable by a process comprising the steps of: 1- selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria, 2- identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates, 3- purifying the polypeptides identified in step 1, which are found in step 2 to be conserved in B2/D isolates, 4- testing the polypeptides for immunogenicity using animals models. Application for making vaccines compositions and immunotherapies



PCT/EP 03/02925

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/31 C12N15/63

G01N33/53

C. DOCUMENTS CONSIDERED TO BE RELEVANT

C07K14/245

C07K16/12

A61K39/108

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE

Category °	Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No.		
Х	WO 01 66572 A (INST NAT SANTE; NASSIF XAVIER (FR); TINSLEY CORNER 13 September 2001 (2001-09-SEQ ID NOs:390 and 391 page 3, line 20 - page 4, line page 29, line 23 - line 31	1-6, 9-13,15, 16	
A	JOHNSON JAMES R ET AL: "Phylogopathotypic similarities between Escherichia coli isolates from tract infections in dogs and extraintestinal infections in JOURNAL OF INFECTIOUS DISEASES vol. 183, no. 6, 2001, pages 89 XP002211433 ISSN: 0022-1899 abstract	n urinary humans."	(
X Furth	ner documents are listed in the continuation of box C.	X Patent family members are listed i	n annex.
"A" docume consid "E" earlier of filing d "L" docume which citation "O" docume other r "P" docume	ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another in or other special reason (as specified) ent referring to an oral disclosure, use, exhibition or	"T" later document published after the interest or priority date and not in conflict with cited to understand the principle or the invention "X" document of particular relevance; the clean of the considered novel or cannot involve an inventive step when the document of particular relevance; the clean of the considered to involve an inventive step when the document is combined with one or moments, such combination being obvious in the art. "&" document member of the same patent for the same patent fo	aimed invention be considered to cument is taken alone laimed invention rentive step when the re other such docu- is to a person skilled
Date of the	actual completion of the international search	Date of mailing of the international sea	rch report
1	1 August 2003	0 5. 12. 2	2003
Name and n	nailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Mata-Vicente, M.	

Form PCT/ISA/210 (second sheet) (July 1992)

PCT/EP 03/02925

		PCT/EP 6	73/02925
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Calegory °	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
A	MUEHLDORFER I ET AL: "Characterization of Escherichia coli strains isolated from environmental water habitats and from stool samples of healthy volunteers." RESEARCH IN MICROBIOLOGY, vol. 147, no. 8, 1996, pages 625-635, XP002211434 ISSN: 0923-2508 table I page 630, paragraph 2		

Form PCT/ISA/210 (continuation of second sheet) (July-1992)

International application No. PCT/EP 03/02925

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210
2. X Claims Nos.: 14 because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: See FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-6, 9-13, 15 and 16 partially
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sneet (1)) (July 1998)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

As far as an "in vivo" method is concerned, claim 9 is directed to a method of treatment of the human/animal body and the search has been carried out and based on the alleged effects of the compound/composition.

As far as an "in vivo" method is concerned, claim 15 is directed to a diagnostic method practised on the human/animal body and the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Claims Nos.: 14

Claim 14 refers to "monoclonal antibodies against epitopes of polypeptide", but it does not say which polypeptide is meant. In consequence, the scope of said claim is ambiguous and vague and its subject-matter is not sufficiently disclosed and supported (Art. 83 and 84 EPC). Therefore, no search has been carried out on said claim.

The phrase "polypeptide such as used according to claim 9" comprised in Claim 13 lacks any sense. Nevertheless, the ISA has assumed that it is an error and that it refers to the polypeptides referred to in Claim 9 or, in other words, a polypeptide selected from the group comprising SEQ ID NOs:1-66 (except SEQ ID NO:8) and 133-145.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims (1-6, 9-13, 15 and 16) - partially

Isolated antigenic polypeptide SEQ ID NO:14; the polynucleotide encoding it (SEQ ID NO:80); vector comprising said polynucleotide and host cell transformed with it; antibodies against said polypeptide; vaccines comprising the polypeptide; methods of diagnosis/treatment derived of the use of any of the molecules previously mentioned.

Inventions 2-32: Claims (1-6, 9-13, 15 and 16) - partially

Idem as invention 1, but restricted to each one of the polypeptides of SEQ ID NOs: 15, 17, 21-23, 28-30, 32, 36, 38, 39, 41-44, 46, 49, 50, 52-55, 58, 60, 63 and 133-138 and their corresponding genes (SEQ ID NOs:81, 83, 87-89, 94-96, 98, 102, 104, 105, 107-110, 112, 115, 116, 118, 119 and 126).

Invention 33: Claims (4-6) - partially

Isolated polynucleotide SEQ ID NO:127, vector comprising it and host cell transformed therewith.

Inventions 34-41: Claims (9-13, 15 and 16) - partially

Idem as invention 33, but restricted to each one of the polynucleotides SEQ ID NOs: 130, 132 and 146-151.

Invention 42: Claims (9-13, 15 and 16) - partially

Use of the polypeptide SEQ ID NO:1 as antigen; vaccines; antibodies against said polypeptide; methods of diagnosis/treatment derived of the use thereof.

Inventions 43-86: Claims (9-13, 15 and 16) - partially

Idem as invention 42, but restricted to each one of the polypeptides SEQ ID NOs: 2-7, 9-13, 16, 18-20, 24-27, 31, 33-35, 37, 40, 45, 47, 48, 51, 56, 57, 59, 61, 62, 64-66, 139-145.

Invention 87: Claims (7 and 8) - completely

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Process for isolating and identifying polypeptides useful as vaccines comprising the steps of: selecting on the basis of sequence analysis those of the polypeptides which are either located in the outermembrane or secreted by the bacteria; identifying the genes coding for said polypeptides which are conserved in B2/D clinical isolates; purifying the polypeptides identified in step 1, which are found in step 2 to be conserved in B2/D isolates; and testing the polypeptides for immunogenicity using animal models.

BNSDOCID: <WO_____03074553A3_I_>

Information on patent family members

manational Application No PCT/EP 03/02925

Patent document	Publication date	Patent family		Publication
cited in search report		member(s)		date
WO 0166572 A	13-09-2001	FR CA WO EP US	2806096 A1 2402602 A1 0166572 A2 1328641 A2 2003148324 A1	14-09-2001 13-09-2001 13-09-2001 23-07-2003 07-08-2003

BNSDOCID: <WO

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